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A STATISTICAL STUDY OF SIX HUNDRED AND SEVENTY-ONE CASES OF APPENDICEAL PERITONITIS*

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INTRODUCTION

OF all the surgical diseases that engage widespread interest, appendicitis is undoubtedly the most familiar. It is not surprising therefore that the literature should be so voluminous, or that it should cover so many different and almost unrelated aspects.

The present study is confined to the clinical problem of peritonitis in patients brought to the hospital for appendicitis. Between 1929 and 1940, the staff of the Massachusetts General Hospital treated 5055 cases of appendicitis, with a mortality rate of 2.04 per cent, but the mortality rate for the 4384 patients without peritonitis was 0.37 per cent, as contrasted with one of 12.97 per cent for the 671 patients who did have peritonitis (Table 1). Great efforts have been and must still be directed toward the earlier diagnosis and treatment of appendicitis, so that this excessive mortality may be avoided, but at the same time one must recognize the facts that there will always be cases of appendiceal peritonitis, and that their management will often be difficult and their mortality discouragingly high. The present study concerns these cases.

TABLE 1. *Incidence and Mortality of All Cases of Appendicitis.*

TYPE OF APPENDICITIS	NO. OF CASES	NO. OF DEATHS	MORTALITY %
Without peritonitis	4384	16	0.37
Acute	2630	14	0.53
Chronic	1754	2	0.11
With peritonitis	671	87	12.97
Acute, without mass	444	71	15.90
Acute, with mass	227	16	7.05
Totals	5055	103	
Average			2.04

The surgeon's hand has been greatly strengthened by the recent progress in chemotherapy, surgical bacteriology, blood chemistry and intestinal intubation, and it is clear that the mortality rate of appendiceal peritonitis is being reduced by their practical application. Our own, for example, has dropped from 25 per cent in 1929 to 6 per cent in 1939, and similar reductions are being widely reported. However, they are only aids and cannot be substituted for clinical judgment and surgical skill. We have therefore concentrated this study on the clinical factors that can be shown to affect the mortality rate of appendiceal peritonitis.

Peritonitis, within the meaning of this study, consists in the presence of gross perforation, pus in the peritoneal cavity or abscess formation as seen at operation or autopsy or as made clear by the clinical course of the disease. Cases wrongly diagnosed have been excluded. Although the absence of gross peritonitis could easily be recognized at operation, we have found it impossible to determine the exact extent without doing a dangerous and unjustifiable amount of exploration. This experience, in addition to the fact that treatment must actually be planned entirely on the basis of the clinical data available before operation, has persuaded us to abandon the purely pathological classifications so often seen in the literature in favor of a classification based on preoperative clinical findings. Of these, we have taken mass formation to be the most fundamental. The presence of a palpable mass gives indisputable evidence of some degree of localization and hence, at least from the point of view of treatment, serves to separate the group in which localization has already occurred from the group in which localiza-

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tion has not and perhaps will not take place. Because these two groups are readily distinguishable clinically and because the treatment differs basically in each, they are classified and reported separately as Parts I and II of this study.

The objection may be raised that such a classification fails to permit any satisfactory comparisons between our figures and those from other clinics where the figures are based on a strictly pathological classification of cases. Our attempts to derive really comparable mortality figures from various published reports have convinced us of the practical impossibility of taking all the relevant factors into account or even of knowing, in any given report, what they were. The essential factors governing the mortality rate of appendiceal peritonitis in any clinic are the type of cases received, the accuracy of clinical appraisal, the policy of treatment and the technical quality of the treatment. If any of these essential factors are ignored, the comparison must be fallacious and misleading. We are therefore less concerned with comparing our mortality statistics with those of others than with trying to find out what factors influenced them and how they may be improved.

During the three years occupied in personally analyzing the records of cases of appendiceal peritonitis admitted to the Massachusetts General Hospital between January 1, 1929, and January 1, 1940, we have also treated or supervised the treatment of all cases of so-called "ruptured appendix." The clinical phase of the study was of value not only in enabling us to investigate new technics but also in forcing us to be realistic in our analysis of the previous records. These records relate to house patients, some of whom were operated on by members of the visiting staff and some by the house staff. The records were uniformly good, although not every one contained all the items of information we sought.

PART I. FOUR HUNDRED AND FORTY-FOUR CASES OF APPENDICEAL PERITONITIS WITHOUT PALPABLE MASS

The patients served by the Massachusetts General Hospital are almost entirely white and mainly comprise city dwellers. Sixty-five per cent of the present group were males. The mortality rate among males was 14.2 per cent, in contrast with 19 per cent among females, perhaps because the presence of peritonitis offered a more difficult differential diagnosis in females and thus led to a relatively higher mortality. The age incidence and mortality by decades (Table 2) of these cases were very similar to those for appendicitis as a whole: the mortality was lowest among young adults, in whom the incidence was highest, and highest among patients at the extremes of life, in whom appendicitis is least common. It is noteworthy, however, that 18 per cent of the 444 patients were infants and children under ten years of age; this suggests that an unfortunately large number of young children with appendicitis are being allowed to progress to the stage of actual peritonitis before being taken to the hospital for treatment. Inherent diagnostic difficulties and the pernicious habit of administering cathartics to fretful children are undoubtedly responsible.

TABLE 2. *Age Incidence and Mortality by Decades.*

AGE	NO. OF CASES	INCIDENCE	NO. OF DEATHS	MORTALITY
yr.		%		%
1–9	79	18	16	20
10–19	154	35	18	11
20–29	69	15	9	13
30–39	35	8	5	14
40–49	43	10	7	16
50–59	33	8	6	18
60 or over	31	7	10	32
Totals	444		71	
Average				15.9

During this eleven-year period, there have necessarily been variations in the technical quality of the treatment and the accuracy of clinical appraisal, as well as in the annual difference in the number and type of cases and progressive changes in the policy of management. No one of these factors alone was responsible for the different annual mortality rates (Table 3), although the types of cases appear to have made the greatest difference, and ironically enough, of all the possible variables this is the one over which we exercise the least control,

TABLE 3. *Annual Distribution of Cases Over an Eleven-Year Period.*

YEAR	NO. OF CASES	MORIBUND OR VERY ILL PATIENTS ON ENTRY	INCIDENCE OF IMMEDIATE APPENDECTOMY	MORTALITY OF IMMEDIATE APPENDECTOMY	MORTALITY OF ALL OTHER TREATMENT	TOTAL MORTALITY
		%	%	%	%	%
1929	28	47	100	25	—	25
1930	28	21	93	23	50	25
1931	54	32	93	12	75	17
1932	54	30	96	15	50	17
1933	40	45	83	18	57	25
1934	34	29	82	14	33	18
1935	36	20	89	9	50	14
1936	77	27	92	4	50	8
1937	27	59	74	20	43	26
1938	35	26	80	4	29	9
1939	31	45	87	7	0	6
Total	444					
Averages		32.7	89.1	12.6	41.7	15.9

since it depends almost entirely on the diagnostic acumen of the medical attendant. That the policy of treatment was rather inflexible during this period is suggested by the consistently high proportion of patients subjected to immediate appendectomy—100 per cent in the highest year and 74 per cent in the lowest, with an average of 89 per cent. In the future, an increasingly flexible policy will be adopted, since it is shown that newer methods not only make appendectomy itself safer but also guarantee the surgeon greater freedom to choose the optimum time for doing it. But this widening scope of free choice, to be successful, implies the exercise of a high degree of clinical judgment and points directly to the importance of an accurate evaluation of preoperative clinical factors in terms of prognosis.

Prognostic Significance of History

Episode Suggestive of Acute Perforation

At some definite time in their illness, one quarter of the 444 patients described a sudden episode that suggested acute perforation of the appendix, and the mortality (25 per cent) among these 115 patients was almost double that (13 per cent) of the 329 patients whose story suggested no definite hour of perforation.

Table 4. *Prognostic Significance of Time of Operation in Ill and Not Very Ill Patients with "Acute Perforation."*

Delay from "Rupture" to Appendectomy	Very Ill Patients			Not Very Ill Patients		
	No. of cases	No. of deaths	Mortality	No. of cases	No. of deaths	Mortality
			%			%
0-5	11	1	9	14	1	7
6-8	14	7	50	14	0	0
9-11	5	2	40	0	0	0
12-17	12	4	33	19	2	11
18-23	7	5	70	2	1	50
24-72	8	5	63	9	0	0
Totals	57	24		58	4	
Averages			42			7

Actually, the prognostic significance of such a story was confined to those patients who looked very ill on admission (Table 4). The mortality rate (42 per cent) was six times higher than that (7 per cent) of the patients who, with or without a history of acute perforation, did not look very ill. The story, the appearance of extreme illness and the high mortality were all presumably due to a relatively sudden gross contamination of the unprotected peritoneal cavity, either from an abrupt parting of protective adhesions or from a massive rupture of an insufficiently walled-off appendix. The patients who did not look very ill presumably did not have this pathologic picture, since so few (7 per cent) of them died. It must therefore be assumed that when patients who do not look very ill give a history suggestive of acute perforation of more than six hours' duration, the symptom probably has no prognostic significance.

In the very ill group, the delay of even six hours (Table 4) between the acute-perforation episode and operation resulted in a mortality rate (50 per cent) five times as great as that resulting from operation within six hours. This mortality rate certainly challenges the wisdom of routine appendectomy under such circumstances. On the other hand, we are not prepared to say that conservative treatment would have resulted better, since this group probably contains most of the cases in which spontaneous localization will never occur. We have not yet had enough experience with appendectomy combined with local chemotherapy to know how effective it will prove in this situation. We do know that in this group every case must be studied individually, and that operation should be elected only after all the significant factors have been weighed. Even then, a predetermined type of appendectomy should be avoided, and full advantage should be taken of whatever additional information is furnished by operative visualization to select the safest further procedure under the circumstances.

Duration of Illness Before Operation

The familiar phrase, "Too late for an early operation, and too early for a late operation," reflects the value that has always been attached to the time element as a guide for safe operation. In this series, the mortality rate more than doubled after the first day of the disease (Table 5) and did not decline until after the fifth day. It is of interest that the postoperative course of the survivors was little influenced by the day of operation, however, even when it fell within the most dangerous period, and this suggests that the day of the disease had much more significance for some patients than for others. The time element therefore served only to point out a group containing patients who would fail to survive appendectomy; it did not

Table 5. *Mortality and Morbidity According to Day of Disease on Which Appendectomy Was Done.*

Day of Disease When Appendectomy Done	No. of Patients	No. of Deaths	Mortality	Incidence of Stormy Convalescence among Survivors	Average Hospital Stay of Survivors
			%	%	*days*
First	79	5	6	34	19
Second	158	23	15	36	20
Third	109	12	11	36	20
Fourth	29	7	24	34	21
Fifth	10	2	20	63	18
After fifth	11	1	9	60	25
Totals	396	50			
Averages			12.6	37	19.8

identify the patients. This ultimate desideratum must depend on an appraisal of all the other significant factors in each case.

Chills

The preoperative occurrence of chills was described in the history of 41 patients, representing a minimal incidence of 9 per cent. These patients suffered a mortality rate of 22 per cent, as compared with a mortality of 16 per cent for the whole group of 444. The proportion of stormy convalescences and the average hospital stay of the 32 survivors did not differ from the average for the whole group. There were 4 recognized cases of pylephlebitis, 3 of which were fatal.

This experience may be summarized by the statement that about one tenth of the patients with appendiceal peritonitis without a palpable mass gave a story of chills, that nine times out of ten it had no prognostic significance, but that the tenth time it meant a probably fatal pylephlebitis.

Previous Attacks

The well-recognized tendency of repeated attacks of appendicitis to increase in severity suggests that peritonitis following a series of attacks should result in a higher mortality than peritonitis complicating an initial attack. It is therefore of some interest that the mortality was about 2 per cent lower in a group of 110 patients who had had repeated attacks than in a similar group who developed peritonitis in their first attack. The difference, though small, suggests that the rapidity and extent of spread of peritonitis may be limited or delayed by the effects of the inflammatory reactions due to previous attacks.

PROGNOSTIC SIGNIFICANCE OF PHYSICAL EXAMINATION

Degree of Illness

The item "general appearance," which appears on the examination sheet in use at the Massachusetts General Hospital, is filled in by the admitting surgeon with a remark — such as "moribund," "very ill," "moderately ill" or "not ill" — that expresses his first impression of the patient's condition. This item has proved to have a more significant relation to the mortality rate than any other single preoperative factor. Reducing the classification to "very ill" and "not very ill," we have found the mortality associated with the former group (33.8 per cent) to have been almost five times higher than that associated with the latter (7.4 per cent), regardless of whether or not immediate appendectomy was carried out (Table 6).

Absent Peristalsis

Definite, complete absence of audible peristalsis in 53 cases was associated with a mortality rate (28 per cent) four times higher than that (7 per cent) of 115 cases in which the peristalsis was definitely present, and almost twice as high as the 16 per cent rate for 25 cases in which the presence of peristalsis was doubtful. As a single measure of lethal degrees of peritonitis, it appeared to rate next in importance to the general appearance of the patient.

TABLE 6. *Mortality in Cases, Variously Treated, According to Degree of Illness on Admission.*

TREATMENT	TOTAL NO. OF CASES	VERY ILL PATIENTS			NOT VERY ILL PATIENTS		
		NO. OF CASES	NO. OF DEATHS	MORTALITY %	NO. OF CASES	NO. OF DEATHS	MORTALITY %
Immediate appendectomy	395	112	30	27	283	20	7
Deferred appendectomy	9	3	0		6	0	
Immediate incision and drainage	13	10	6		3	1	
Deferred incision and drainage	16	13	6	58	3	0	14
No operation	11	7	7		4	1	
Totals	444	145	49		299	22	
Averages				33.8			7.4

Abdominal Spasm

In 215 cases, spasm was described as diffuse or generalized, and the mortality was 21 per cent. This was twice as high as the 10 per cent mortality suffered by 199 patients with only local spasm, and over three times higher than that (6 per cent) of 16 patients who had no abdominal spasm at all. Thus, on the basis of 430 cases, the extent of spasm appeared to be the third most significant factor in the physical examinations.

Rectal Tenderness

Almost twice as many (21 per cent) of the 70 patients who did not have rectal tenderness died as of the 277 patients who did (13 per cent). This rather surprising relation suggests that the direction in which the peritonitis spreads is perhaps of more significance than its actual extent, and such an explanation fits in with the well-recognized ability of the pelvic peritoneum to resist infection.

PROGNOSTIC SIGNIFICANCE OF LABORATORY DATA

Leukocyte-Pulse Index

That the original temperature, pulse and leukocyte count have more than a diagnostic significance

is generally appreciated, but just how and to what extent they may be used as an aid to prognosis and treatment is less well understood.

There is ample reason to believe that an abnormally rapid pulse in a patient with peritonitis is a measure of toxicity, whereas an accompanying leukocytosis reflects the degree to which the patient can mobilize his cellular elements to resist infection. (The significance of temperature variations is less clear, but it appears roughly to parallel that of the leukocyte count.) The relation between the amount of leukocytosis and the rapidity of the pulse might therefore be expected to represent the relative strength of the forces of destruction and of protection and hence to have a direct bearing on the prognosis of the case. In the absence of acute sepsis, such a concept would, of course, have no meaning.

We have attempted to express this relation by dividing the thousands of the leukocyte count into the pulse rate, to obtain a single number, which may be called the "leukocyte-pulse index." It might have been possible, by mathematical manipulations, to cancel the normal element from both components and thus obtain a truer expression of the significant relation, but we have refrained in the interests of simplicity. For example, with a leukocyte count of 20,000 and a pulse rate of 100, the index is 100 divided by 20, or 5.

TABLE 7. *Relative Prognostic Value of Various Clinical Factors as Determined by the Mortality Rate Associated with Each Factor, Based on 444 Cases with a Total Mortality of 15.9 Per Cent.*

CLINICAL FACTOR	MORTALITY WITH FACTOR PRESENT	MORTALITY WITH FACTOR ABSENT
	%	%
Story of "acute perforation" in very ill patient	42	7
Patient very ill on admission	34	7
Peristalsis definitely absent	28	9
Wrong preoperative diagnosis	33	15
Age over sixty years	32	15
Peristalsis not definitely present	23	7
Leukocyte-pulse index above 6	21	6
Story of "acute perforation"	25	13
Abdominal spasm diffuse	21	10
Operation not on first day of disease	18	7
Age below ten or above sixty years	24	13
Abdominal spasm present	16	6
Rectal tenderness absent	21	13
Story of preoperative chills	22	15
Age under ten years	20	15
Female sex	19	14
First attack of appendicitis	13	11

In tabulating the average figures for living and dead patients, we have used the preoperative data of 335 patients subjected to immediate appendectomy, omitting the 27 patients over sixty years of age because they showed a rather different relation and yet were too few to permit an adequate investigation of this variation. The 292 patients who survived tended to have more leukocytosis in relation to their pulse-rate than the 43 who succumbed; the leukocyte-pulse index averaged below 6 for the survivors and above 6 for the fatalities, and children had the same relation as adults but based on higher counts. From these averages, we have taken 6 to represent the critical point in mortality prognosis.

The mortality for patients with a leukocyte-pulse index below 6 was 6 per cent, but for those having an index above 6 it was 21 per cent, or more than three times as great (Table 7). This difference is large enough to exclude coincidence, so that a definite prognostic significance may be attached to it in cases of acute appendiceal peritonitis without mass formation.

Other Laboratory Data

Routine urine examinations were done, but we have not included them except to note how often blood cells appeared in the sediment as a possibly confusing diagnostic factor. Red cells were found in 19 cases and white cells in 70. We examined catheter specimens of female patients to be certain that the cells originated in the urinary tract.

Differential blood counts and other special procedures were omitted from this study, since there were too few for useful analysis. We believe that they should be done whenever the clinical diagnosis is in doubt.

PROGNOSTIC SIGNIFICANCE OF DIAGNOSTIC ERRORS

As mentioned above, we have eliminated those cases in which the diagnosis of appendiceal peritonitis was proved to be wrong. Most of them were uncomplicated acute appendicitis without gross peritonitis and were treated by immediate appendectomy, and the patients did well, as would be expected in the early stages of the disease. So far as we could tell, no patient was allowed to rupture his appendix in the hospital because of the mistaken idea that it had already ruptured and should therefore be treated conservatively. The danger of falling into this error must be recalled, however, when the choice of deferring operation is under consideration.

The only diagnostic errors included in this study occurred in the cases that were actually appendiceal peritonitis but were mistaken for something else. There were 18, of which 6 were fatal, a mortality of 33 per cent, which is more than double that for the 426 correctly diagnosed cases. The mistaken preoperative diagnoses were perforated peptic ulcer in 5 cases (2 fatal), diagnosis in doubt in 4 cases (2 fatal), acute salpingitis in 3 cases (1 fatal), acute unruptured appendicitis in 2 cases, acute hepatitis in 1 fatal case, and acute cholecystitis, acute pancreatitis and ovarian carcinoma each in 1 case.

It is apparent that these errors affected the mortality prognosis unfavorably only so far as the misdirected treatment of each patient was incompatible with recovery from acute appendiceal peritonitis.

Summary of Prognostic Preoperative Factors

Table 7 presents some of the factors that are familiarly thought of in terms of pathology but could be more directly used as guides for the selection of treatment if they were interpreted in terms of prognosis. An attempt has been made to arrange them in the order of their prognostic significance, the mortality rate of two groups of similarly treated patients being contrasted; one group was characterized by the presence of some factor, and the other group by its absence. It is realized that no such correlation can be taken too literally because the contrasted groups could not be identical in every particular save the one under consideration.

We believe that when several of the most unfavorable factors are combined in one case, the patient must be recognized as an extremely bad risk, and that particular care must be taken in selecting the safest treatment.

Influence of Treatment on Mortality Rate

Choice of Treatment

At the Massachusetts General Hospital during most of the period covered by this study, the policy favored immediate operation at any stage of the disease, provided only that the patient appeared strong enough to stand the operation. More recently, the wisdom of operation in the presence of gross peritonitis has been increasingly questioned, particularly since the newer methods of controlling ileus, distention, fluid imbalance and infection have increased the efficacy of expectant treatment.

The fact that immediate operation was chosen in 91.9 per cent of our cases (Table 8) — even for 84 per cent of the patients who were very ill or moribund (Table 6) — reflects the nature of the policy then in force, and the mortality of 14 per cent seems remarkably low in view of the fact that one third of the patients were very ill at the time of operation. By contrast, the small group selected for expectant treatment was largely (two thirds) composed of very ill or moribund patients, and that this group should have suffered a 39 per cent mortality rate is not surprising.

Evidence of a gradual change of policy may be found in the annual figures (Table 3). The proportion of patients subjected to immediate appendectomy in the presence of peritonitis declined from 100 per cent in 1929 to 87 per cent in 1939, with a parallel decline in the mortality rate from 25 to 6 per cent. We believe that this shift in policy and improvement in the mortality figures was partly due to an increasing recognition of the value of accurate individualization.

Table 8. *Mortality According to Choice of Treatment.*

Treatment	No. of Cases	Incidence %	No. of Deaths	Mortality %
Immediate operation	408	92	57	14
Immediate appendectomy	395	89.1	50	12.6
Immediate incision and drainage alone	13	2.7	7	54
Expectant treatment	36	8	14	39
Deferred incision and drainage alone	16	3.6	6	38
Deferred appendectomy	9	2.0	0	0
No operation	11	2.6	8	73
Totals	444		71	
Average				15.9

Technical Factors

It is apparent that the different degrees of technical skill of the surgeons who operated on the patients in this series must have had a significant effect on the mortality rate, but one that would be extremely difficult to calculate or to control. It has been profitable to examine certain technical factors, however.

Type of incision. For purposes of comparison, we have divided incisions into two main types, lateral and medial. The former refers to the relatively small gridiron incisions, as described by McBurney and Rockey, characterized by a minimal exposure of small bowel. The medial type includes midline, paramedian, rectus-splitting and rectus-retracting incisions, all characterized by a greater exposure and manipulation of viscera, especially small bowel.

Appendectomy was seldom done through a McBurney type incision, and its use in cases without a mass appears to have made no difference in the mortality rate. The survivors of appendectomy had an identical incidence of stormy convalescence (36 per cent) and averaged

an identical number of hospital days (twenty), regardless of the type of incision used.

The choice of incision appeared to make a great difference in the 26 cases of incision and drainage without appendectomy: the mortality was almost three times higher when a median type of incision was used (Table 9). Again, the survivors had an identical incidence of stormy convalescence (40 per cent), regardless of the type of incision, which is perhaps only another way of saying that the patients did or did not get fatal general peritonitis as a result of surgical manipulations.

We believe that trauma to peritoneal surfaces with gauze packs, breaking down of protective adhesions and contamination of uninfected areas of the others depended largely on the current popularity of one or another type.

Obviously, the correct choice of the anesthetic for every case is important, and if in every case the technic of its administration could be perfect, the correct choice would be solely a matter of correctly evaluating each patient. But faulty technic, resulting in an adequate degree of relaxation for the gentle, careful, safe sort of surgery that is essential in appendiceal peritonitis, may make any choice wrong. The correct choice must therefore depend partly on the quality of the available anesthetist, partly on the nature of the proposed operation, partly on the technical capabilities of the surgeon, and partly on the patient's physical and

TABLE 9. *Type of Incision and Associated Mortality.*

OPERATION	MEDIAL-TYPE INCISION			LATERAL-TYPE INCISION		
	NO. OF CASES	NO. OF DEATHS	MORTALITY %	NO. OF CASES	NO. OF DEATHS	MORTALITY %
Appendectomy, immediate	360	45	13	32	4	13
Appendectomy, deferred	5	0	0	3	0	0
Incision and drainage alone	17	10	59	9	2	22
Totals	382	55		44	6	
Averages			14.4			13.6

increase the mortality rate regardless of the incision through which such offenses are committed. They were absolutely inexcusable in the performance of simple drainage, in which adequate exposure was not a consideration. In appendectomy, on the other hand, the demands of adequate exposure and avoidance of fatal trauma had to be reconciled, and the care and skill of the surgeon were apparently of greater consequence than the type of incision.

The medial type of incision is frequently advocated for females for convenience in reaching the pelvic organs, should they prove to be the true source of the symptoms. There is no objection to this in the absence of peritonitis, but it may result badly when gross appendiceal peritonitis is present. When the presence of peritonitis is in doubt, two incisions are safer than one disastrously wrong one.

Anesthetic. No deaths could be definitely attributed to the anesthetic, but poor choice and poor administration undoubtedly contributed to some of them. Ether (287 cases), spinal (115 cases) and local (28 cases) anesthesias were most frequently chosen. How much the mortality associated with each type relates to the anesthetic and how much it reflects the sort of cases in which each was used cannot be determined. The specific reasons for choosing a spinal anesthetic in 23 cases and a local in 28 cases were recorded, but the choice in most mental condition. We are convinced that these considerations fundamentally influence the mortality rate, but unfortunately they cannot be expressed in terms of statistics.

Length of operation. The time from the skin incision to the application of the dressing was accurately recorded in 392 appendectomies. The 392 operations averaged forty-nine minutes and resulted in a mortality of 12.6 per cent.

As might be expected, the mortality was higher among very ill patients (26 per cent), even though their operations averaged only about five sixths as long as those of not very ill patients. Comparing the average length of operations that resulted in death and in recovery, it was seen that among good-risk patients long operations were associated with death and shorter operations with recovery, whereas among very ill patients the shorter operations were followed by death and the longer ones by recovery. It is thus clear that there is no simple relation between length of operation and mortality. A comparison of the actual mortality rates for each length of operation shows that the shortest operations did not have the lowest mortality rates among either the very ill or the not very ill patients. In both groups, the lowest mortality was for operations lasting between fifty and sixty minutes, and after one hour the mortality rate began to rise (Table 10).

We may safely assume that what determined

the length of these operations was how difficult the removal of each particular appendix proved for the particular surgeon, in addition, of course, to his own estimate of the need for haste. When the combination resulted in a degree of damage from which recovery was impossible, the patient died. Viewed in this light, our figures mean that speed is not in itself desirable, that avoidance of trauma is essential, and that if an appendix cannot be removed without undue trauma in one hour it should not be removed by that surgeon at that operation.

The length of 83 appendectomies in children under eleven was thirty-six minutes, and the mortality was 15 per cent. Possibly, safe appendectomy can be done more rapidly in children than in adults, but in the presence of peritonitis children tolerated rapid (and therefore perhaps rough) appendectomies no better than adults.

Use of drains. The time has passed when the surgeon at operation can fall back on some simple rule of thumb such as "When in doubt, drain" or "When in doubt, do not drain" and be satisfied that he has done the best thing for the patient. In view of the controversial opinions in the literature on the theoretical value of drainage, he cannot be blamed if he finds himself in doubt most of the time. With so many conflicting views advanced, there may be some practical value in noting the actual effects that could be attributed to the use of drains in the present cases.

Drains were used in the vast majority (96 per cent) of the 433 operative cases. Pus was removed by the suction tip, and two drains were placed most frequently (258 cases), one in the pelvis and one lateral to the cecum. Less frequently (128 cases), only one drain was used, either lateral to the cecum or in the pelvis. Three drains were used in 20 cases, and four drains in 9 cases.

An attempt was always made to avoid having any drain in contact with the small intestine or appendix stump. For this reason, it was thought desirable in 55 cases to bring the drain or drains out through a stab wound rather than through the main incision. Intestinal obstruction developed in only 8 (2 per cent) of the 415 drained cases, and was fatal in only 1 case (0.2 per cent).

In 18 cases, the abdomen was closed without drainage. Two of these patients were very ill, and 16 were not very ill, at the time of operation. All 18 recovered. One developed intestinal obstruction, which required operation on the seventh day after appendectomy. Three others developed a residual abscess requiring drainage. Five had a stormy, prolonged convalescence, and the remaining 9 did well.

On the basis of this experience, we must conclude that properly placed cigarette drains do little or no harm, and that we have no evidence that would justify omitting them in cases of gross appendiceal peritonitis merely as a matter of policy.

Other factors. In recent years, blood transfusions have been given with greater frequency. In all, 51 of the 444 patients were transfused, each of these patients averaging two transfusions. Twenty-two patients died, and 29 recovered. These were obviously the sickest patients.

Chemotherapy was used successfully in 4 of the more recent cases covered by this report. Although it is now being used with increasing frequency, we have not had sufficient cases for useful analysis.

Smears and cultures may also assume greater importance as aids to treatment and prognosis, but since their full value was not appreciated during the earlier years covered by this study and since the laboratory methods have been changing and improving, we are not in a position to include this very interesting aspect of treatment.

There can be no question that part of the recent improvement shown by our own mortality figures and by those of others is due to improved methods of postoperative care based on more efficient therapeutic apparatus and better understanding of applied biologic chemistry. These factors, however, do not lend themselves to the statistical method of analysis, and we have therefore not attempted to

TABLE 10. *Mortality Rate for Each Length of Operation According to Degree of Illness in Cases of Immediate Appendectomy.*

Length of Operation	Very Ill Patients			Not Very Ill Patients			All Patients		
	No. of cases	No. of deaths	Mortality	No. of cases	No. of deaths	Mortality	No. of cases	No. of deaths	Mortality
min.			%			%			%
20 or less	5	2	40	6	1	17	11	3	27
21–30	25	9	36	40	3	8	65	12	19
31–40	28	7	25	62	3	5	90	10	11
41–50	20	6	30	58	3	5	78	9	12
51–60	23	3	13	60	3	5	83	6	7
Over 60	10	2	20	55	8	15	65	10	15
Totals	111	29		281	21		392	50	
Averages			26			7.5			12.7

evaluate them as we have certain other technical factors concerned with the mortality rate.

Complications

Residual abscesses following appendectomy (5 undrained, 35 drained) were encountered in 40 cases, with 4 deaths and an average of thirty-three hospital days for the survivors. Spontaneous resolution of the abscess took place in 20 cases. In the other 20, abdominal incision and drainage was necessary in 16, rectal puncture in 4. Nonfatal pneumonia was seen in 4 cases, and pneumonia was present in 8 cases of fatal peritonitis. Pulmonary infarcts were recognized in 2 cases, the patients averaging twenty-seven hospital days. Pulmonary collapse in 10 cases did not increase the length of hospitalization. There seemed to be no correlation between these pulmonary complications and the type of anesthesia.

There were 24 cases of major wound sepsis, 1 of wound dehiscence, and 1 of hemorrhage from the wound, all in drained cases, resulting in an average hospital stay of twenty-six days. Fecal fistula developed in 3 cases, with an average hospitalization of forty-four days, and all closed spontaneously. Two incisional hernias were noted, both following drained rectus-retracting incisions.

Nine cases of intestinal obstruction developed; 1 was fatal, and the other 8 resulted in an average hospital stay of thirty-eight days. Six of these patients had ileostomy done to relieve serious obstruction, since the Miller–Abbott tube was not then available.

Phlebitis lengthened the hospital time to twenty-seven days in 2 cases.

There was 1 case each of nonfatal pylephlebitis, urinary fistula, empyema, herpes zoster and pulmonary embolism, the hospital stays varying from one hundred and seventeen to seventeen days but averaging well above the nineteen-day period that was the average for the whole group.

Causes of Death

Of the 71 deaths, 49, or almost 70 per cent, were caused by general peritonitis, with or without such concomitant complications as pneumonia in 8 cases, intestinal obstruction in 3, septicemia in 1 and massive wound sepsis in 1. Six deaths were caused by pneumonia, with concomitant diabetes in 1 case and wound sepsis in 1. Three were caused by pylephlebitis, and 3 by pulmonary embolism. Sepsis, subphrenic abscess, gas gangrene, uremia, acute nephritis, right heart dilatation, myocardial failure and acute respiratory failure each caused death in 1 case; there were 2 undetermined causes, 1 of sudden death on the operating table and 1 of epileptiform convulsions six hours after operation, no autopsy being performed.

Preventability of Deaths

We have studied the records of the fatal cases to see if any of the 71 patients could have been saved by different management in the hospital. This is not easy to ascertain, since a number of elements, some of them unknown and indeterminate, combined to produce each death. We have, however, tried to pick out the cases in which some error that is known to be frequently fatal may have been made.

Errors in Diagnosis

Two patients were explored through an upper abdominal incision for perforated duodenal ulcer a few hours after onset of symptoms, and both died of general peritonitis caused presumably by manual dissemination of pus from a ruptured appendix. This disaster would have been averted if the appendix had first been explored through a small incision in the right lower quadrant.

A nineteen-year-old girl at autopsy showed coexistent chronic salpingitis and ruptured appendix, with general peritonitis. She had entered the hospital on the first day of her acute symptoms, and had been treated conservatively for pelvic inflammation.

One woman entered the hospital in premature labor with atypical pain, died without operation, and at autopsy showed a ruptured appendix, with general peritonitis.

A child was studied for eleven days on our children's medical service, died without a diagnosis, and was found at autopsy to have a ruptured appendix and general peritonitis.

These were undoubtedly all difficult diagnostic problems, and similar ones are constantly being seen. Since appendicitis is by far the commonest abdominal emergency, we believe gentle exploration through a small McBurney incision to be justifiable whenever the presence of a ruptured appendix cannot be excluded and the contemplated treatment is incompatible with recovery from appendiceal peritonitis. We have frequently attempted to aspirate the peritoneal cavity in doubtful cases, with no ill effects so far, but a negative result is of no diagnostic significance, and the procedure cannot be regarded as free of risk.

Wrong Choice of Treatment

Eleven of the appendectomies that were done between the third and the seventh day of the disease were fatal, the patients dying of general peritonitis. We cannot say that this was a wrong choice of treatment in these particular cases, but we can point out again that this is the phase of the disease in which appendectomy carries the highest mortality, when localization is trying to

take place, and when trauma to the peritoneal cavity is likeliest to be harmful. We are not convinced, however, that this dangerous period can be recognized by the day alone. All the data that reflect how well or how badly the patient is handling his infection must enter into the decision, as must the surgeon's personal ability to do a nontraumatic operation. Certainly, no oversimplified rule can be blindly followed as a guide to treatment. We believe that some of these 11 fatalities could have been prevented by a choice of treatment better fitted to the clinical indications.

Prolonged Surgery

Five deaths followed appendectomies lasting from seventy to one hundred minutes. Only 1 of the patients was very ill before operation, yet all 5 died of either peritonitis or pneumonia within five days. We question the judgment of persisting beyond one hour with a difficult appendectomy in the presence of peritonitis. The temptation is all too great, especially among the younger surgeons, to allow personal considerations of pride to obscure the main issue of the patient's welfare, once appendectomy has been started. Some of these deaths might have been avoided had the surgeon made a gentle investigation, satisfied himself that appendectomy would be technically difficult and time-consuming, and then elected the lesser risk of draining the region of the appendix and ochsnerizing the patient until a safer time.

Errors in Technic

Six patients who were not very ill before operation nevertheless died promptly of general peritonitis following operations that were neither unduly prolonged nor unwisely timed. The presumption is that rough handling, unnecessary exposure of intestines, unjustifiable packing of gauze into the abdomen and other technical crudities resulted in breaking down delicate protective barriers, with resultant wide dissemination of sepsis in the peritoneal cavity. To whatever extent these presumptions are true must the above six deaths be considered avoidable deaths.

Unavoidable Deaths

Fourteen deaths apparently could not have been prevented. Ten patients were moribund on admission and failed to respond to Ochsner treatment reinforced by transfusions, Wangensteen drainage and other well-chosen efforts. Four other patients died during convalescence from successful operations, 3 of pulmonary embolism and 1 of acute nephritis.

Nineteen deaths were probably unavoidable, although not so clearly so as the above. This group comprised deaths from pneumonia, pylephlebitis, gas gangrene, septicemia, epileptiform convulsions, acute respiratory failure, acute cardiac failure and peritonitis.

The remaining 11 deaths may or may not have been preventable, the circumstances admitting no presumption either way.

In conclusion, it should be emphasized that all 71 deaths were avoidable in the sense that earlier diagnosis and treatment of the 444 cases of acute appendicitis would have obviated the dangerous and difficult problems of peritonitis and its complications.

Summary and Conclusions

The use of a clinical in place of a pathological basis of classification in a statistical review of 444 cases of appendiceal peritonitis without palpable mass formation has furnished guides for more accurate appraisal and hence more satisfactory individualization of treatment in such cases.

The great majority of deaths are due to progressive generalized peritonitis. The ability to recognize in advance the cases in which localization will or will not take place and to select the safest time for operation in each case, together with good preoperative and postoperative care and a minimum of trauma to the peritoneum, will determine the success of treatment.

The following conclusions seem justifiable:

Patients who look ill on admission and are operated on more than six hours after an incident interpreted as an acute perforation suffer the highest mortality (50 per cent).

A general appearance of being very ill is the most unfavorable prognostic sign, and absence of audible peristalsis is next in importance.

A pulse rate too rapid for the leukocyte count that accompanies it (leukocyte-pulse index over 6) is the most unfavorable prognostic laboratory observation.

The fourth and fifth days of the disease are the most dangerous for appendectomy (22 per cent mortality), the first day is the least (6 per cent). After the fifth day the mortality diminishes to about 9 per cent.

For incision and drainage alone, the McBurney type of incision is more than twice as safe as a medial type of incision. For appendectomy, the type of incision is of less consequence than the amount of trauma done through it.

About half the residual abscesses following appendectomy regress spontaneously.

Appendectomy lasting between fifty and sixty minutes results in about half the mortality rate of either longer or shorter operations.

The proper use of cigarette drains is satisfactory and safe.

When the diagnosis is in doubt and the contemplated treatment is incompatible with recovery from acute appendiceal peritonitis, a fatality may sometimes be avoided by a preliminary gentle exploration through a small McBurney incision.

(To be concluded)

BOSTON MEDICAL LIBRARY

REPORT OF THE PRESIDENT FOR THE YEAR 1941*

ALTHOUGH there appears to be no definite provision in Article XVI of the by-laws, which prescribes the order of business at the annual meeting, for a communication from the president, perhaps under "Incidental Business" it may be appropriate for him to report on the "State of the Library" with a view especially to telling of the needs and planning for its greater usefulness and prosperity in the future.

He who attempts to appraise an institution without first exploring its history is likely to fail truly to understand its character and significance, and I should therefore like to recommend to all of you as "required reading" the fascinating account by our late Librarian, Dr. Farlow, of the efforts, during one hundred and fifty years, of the physicians of Boston to secure the advantages of a medical library. With the passion of our forebears for education, it is likely that, quite unknown to us, groups were formed to share the half dozen medical and scientific journals, and the few medical volumes brought to this country from abroad. The Medical Improvement Society, organized in 1803 by men many of whose surnames may be found on our roster of today, gathered together books that they held under a statute of 1798 as the Second Social or Boston Medical Library; these volumes were housed at Dr. John Fleet's, and a little later at the apothecary shop of Amos Smith, 39 Marlboro Street (now near the corner of Washington and Milk streets). Among the moving spirits, as anyone would predict, were young John C. Warren, treasurer and later librarian, and his friend James Jackson. A list of the books at this time shows twenty-nine titles. Young Dr. Warren was giving a course in anatomy in rooms over White's apothecary shop at 49 Marlboro Street (Washington Street, near the corner of Franklin), and since he was librarian of the little library, it was natural that the books should be moved there from Smith's apothecary shop. At about this time, 1810, the Harvard Medical School, consisting of the persons of Dr. John Warren, Sr., Dr. Benjamin Waterhouse and Dr. Dexter and their lecture notes, was transferred there from Cambridge. Moreover, Dr. Thomas I. Parker, who had become librarian of the little collection, had his private office at the same address. Later, in 1819, after the medical school had moved to Mason Street, the Boston Medical Library accompanied it to that building, so that it was housed and doubtless closely identified with the school at these two locations, and probably in the latter building was actually united with whatever books had been collected by the Massachusetts Medical College, as the future Harvard Medical School was then called. But the faculty, for reasons now unknown, apparently allowed the alliance to lapse, and in 1826 the accumulated two thousand volumes of the Boston Medical Library, appraised at $4500, were conveyed to the Boston Athenaeum, which was absorbing various circulating libraries of Boston to enrich its collections, and the thirty-one physicians who, of the seventy-one in Boston, were members of the Library became proprietors of the Athenaeum. Thus, after an adventurous existence of twenty-three years, the Boston Medical Library lost its corporate identity, and even its name lapsed as designating a group of books on medical subjects in the Athenaeum. At least two other futile attempts — one by the Observation Society in 1848 and another by the Suffolk District Medical Society — to start a library indicate the need felt by Boston physicians for such an institution.

This was the situation when Dr. James R. Chadwick, thirty years of age, recently returned from Europe, became obsessed with the idea that some at least of the advantages of study abroad could be secured for the doctors of Boston by the establishment of a working and reference library. A preliminary meeting was held on December 21, 1874, and a second meeting one week later, at the office of Dr. Henry I. Bowditch. Final organization was accomplished on August 20, 1875. With the names of those present as a text might be written the history of medicine

*Read at the annual meeting of the Boston Medical Library, March 3, 1942.

in Boston: Bowditch — anti-slavery agitator, co-discoverer with Dr. Morrill Wyman of paracentesis of the thorax, one-time Jackson Professor of Clinical Medicine, founder of the Society for Medical Improvement — was the first chairman of the first board of health established by any state in the Union; Oliver Wendell Holmes was Parkman Professor of Anatomy and already a great figure among New England literati; Samuel A. Green had a splendid Civil War record and was a historian, a man of letters and later to be mayor of Boston; and Francis Minot was Hersey Professor of Theory and Practice. Associated with these elder statesmen of medicine was a group of younger men of from thirty to forty years of age, including Thomas Dwight, F. I. Knight, R. T. Edes, Henry P. Bowditch, Clarence J. Blake, Charles P. Putnam, C. E. Stedman, William L. Richardson, Edward H. Wigglesworth, Reginald H. Fitz, Francis W. Draper, E. J. Forster, James B. Ayer, A. Lawrence Mason and Oliver Wadsworth — young, enthusiastic, almost to a man destined for high teaching positions, often of professorial rank, in the Harvard Medical School. Holmes was chosen president, Wadsworth secretary, Mason treasurer, and Chadwick librarian.[1]

In October, 1875, two rooms in the basement of 5 Hamilton Place, opposite the Park Street Church, were secured and fitted with two tables, thirteen chairs and some bookshelves. Chadwick's zeal secured the exchanges of the *Boston Medical and Surgical Journal* and the collection of the Society of Medical Observation; the libraries of Dr. George Hayward, clinical professor of surgery, Edward H. Clarke, professor of materia medica, and George Cheyne Shattuck, founder of the Shattuck Professorship of Pathological Anatomy, poured in and were piled on the floor. Soon, there was scarcely room for readers, and the invincible enthusiasts begged and subscribed more money, placed a mortgage and purchased a little house at 19 Boylston Place, once the home of the philanthropist, Dr. Samuel Gridley Howe and his wife Julia Ward Howe. At the dedication ceremonies on December 3, 1876, addresses were made by the president, Dr. Holmes, Dr. John Shaw Billings, librarian of the National Medical Library in Washington, Professor Justin Winsor, librarian of Harvard College, Dr. George H. Lyman, president of the Massachusetts Medical Society, Dr. Calvin Ellis, dean of the Harvard Medical School, Charles W. Eliot, president of Harvard College, and Dr. Henry I. Bowditch. These names are set down as the best indication of the importance ascribed to the occasion by the intellectual leaders of the community.

In the new location, more accessions poured in. From the Massachusetts Medical Society came fifteen hundred items; from the library of Dr. J. Orne Green, seven hundred volumes; from the Harvard Medical School, its collection of periodicals and many books, in exchange for duplicate textbooks; and from Dr. Calvin Ellis, late professor of clinical medicine and dean of the Harvard Medical School, his valuable library. By 1886, ten years after removal to the new location, the building was becoming overcrowded. Drs. F. C. Shattuck and Charles R. Putnam established a directory of nurses, which found office space in the library, for which it paid a welcome rental. The councilors of the Massachusetts Medical Society began to meet in the reading room. A possible solution was seen in the proposed inclusion of the library in the new building of the Harvard Medical School at the corner of Boylston and Exeter streets, but the project was not deemed feasible. When Holmes, three years before his death, presented nearly a thousand volumes and caused to be built the bookcases to house them, when the Boston Athenaeum gave its entire medical collection, including the two thousand volumes formerly belonging to the Second Social or Boston Medical Library, which had reposed on its shelves for seventy years, and when the libraries of Edward Wigglesworth, Henry J. Bigelow, Conrad Wesselhoeft and many volumes from the Warren family were added, the problems of overcrowding and of financial support became as acute as ever. How these were solved for a time by generous gifts and bequests and by the building in 1900 of our present splendid house on the Fenway, how we have been enriched by the William Norton Bullard and by the Hyams collections of incunabula and manuscripts, and how portraits, engravings, letters, medals and medical memorabilia have been entrusted to us for posterity constitute a story too long to tell here. Our plant cost half a million dollars; our books and treasures are carried at an equal sum, but are, of course, actually irreplaceable. We stand fourth among the medical libraries in America.

Our past, at least is secure, but what of the future? It occasions your trustees grave anxiety. The Library looks well nourished and presents — with some reservations — an outward appearance of health, but its intimate advisers know that it is anemic and that its vital organs are suffering from financial anoxia. It is operated on an annual income of less than $32,000 of which less than half is income from an endowment that has suffered serious capital depletion, less than a third is from dues, and the rest is from rental of space and from gifts and miscellaneous sources. We have never been able to complete the stacks, periodical room and other facilities for which our new addition — built with funds raised by the campaign of 1929-1930 — was designed. Thousands of books are

piled in the basement awaiting shelving or other disposition, hundreds of volumes of periodicals are unbound and wrapped for preservation in paper or temporary covers. Thousands of bindings should be renewed. Our salaried staff — but five in number — are numerically inadequate, devoted though they are. Our director, completing his fiftieth year of continuous service, must be supposed to be mortal, — ageless though he seems, — and his accumulated experience and knowledge should be communicated to a young associate. Our fellows — now some eight hundred in number, have diminished by one hundred during the past year. Most of them have shown a loyal spirit of support, like the late George Craigin, who — although long retired — rounded out fifty years of membership, finally terminated by his recent decease. But surely there must be twice as many physicians in Greater Boston and New England who would offer support did they realize our need. Perhaps our very liberality in opening our doors and reading rooms to any reputable citizen, whether or not a physician, has lightened our purse. Furthermore, our marrow has been stimulated recently by radical therapy, which — however optimistic we may be — must be considered fortuitous and not dependable so far as the future is concerned. The bequest of $25,000 by Dr. Holmes's daughter, subject to a life interest of her brother, Justice Holmes, became available recently and was devoted to the payment of debts and to needed renovation of our building; half the $10,000 bequest of Dr. John W. Farlow, our second librarian, was spent on repairs; two thirds of a similar sum, a gift from the family of our first secretary, Dr. Oliver F. Wadsworth, and of his son Richard — a later treasurer — was used in renovation and furnishings, and most unpredictable of all, the WPA carried out a splendid project of sorting, classifying, cleaning, cataloguing, boxing and shelving that represented a money value of $75,000. Idle hands now find other occupation.

Perhaps, in these paragraphs, you have gained a true impression of our library in its earlier years, as an institution sorely needed by the closely knit medical profession of its time, supported by the mental and actual manual labor and by the purses of most of the physicians of Boston who amounted to anything, closely associated with the Harvard Medical School and its graduates because there were no others, and subject to no rivals as a source of medical literature. Great changes that have since occurred pose new problems. Fortunately for Boston and New England and the world at large, the medical schools of Boston University and of Tufts College have been born and have prospered, and each takes pride in a working library of its own. That of the Harvard Medical School — necessarily with powerful support — has grown by leaps and bounds. Each hospital maintains its library for the use of staff and interns and nurses. Moreover, the individual physician receives from two to ten or more periodicals, — depending on the societies to which he belongs and his special interests, — which, with their abstracts, supply him with all the current medical information he can absorb. There is danger of — indeed there exists — duplication of effort, which is wasteful, and division of support, which is unfortunate. Let it be emphasized, however, that among the various medical libraries exists cordial co-operation: several hold "professional membership" in our library and constantly make use of the privilege of supplementing their books of reference.

Confronted by these facts and tendencies as they have developed over the years, your trustees have given serious consideration to various proposals, involving usually some form of alliance or amalgamation, with increased opportunity for service. Sixteen years ago, a plan for an academy, with our library as its nucleus, advanced to a point where a charter was obtained, and tentative plans were drawn. Of this project and the reasons for its failure, your president has no personal knowledge. Once more, however, the subject is ripe for review, especially because there is available an illuminating survey of the medical libraries of Boston, with recommendations for the future, from an authoritative source.

Through the good offices of the director of the Harvard University Library, the Carnegie Corporation financed the commission of Mr. Thomas P. Fleming, medical librarian of the College of Physicians and Surgeons of Columbia University, to examine all our medical libraries, to confer with a committee and make a report with recommendations. The work was done during the summer and autumn of 1941. Mr. Fleming made an elaborate factual survey of eleven libraries, with their many subordinate units, and the committee made a report that has been appropriately distributed. The findings that especially concern us are as follows:

> That the Boston Medical Library is centrally located and has sufficient storage space for many years to come; . . . that because of lack of funds it is understaffed and does not furnish the type of service, in regard to either quantity or quality, that is to be expected; . . . that its future — particularly in view of present-day attempts to eliminate decentralization and duplication — hinges about its development as a *reference library*, not only for the benefit of Boston and its immediate vicinity but also for the rest of Massachusetts and other New England states.

The recommendations made by the committee include:

> That the staff of the Boston Medical Library be increased, to provide adequate and efficient service; . . . that all working libraries co-operate with it . . . and use it to best advantage as their reference library; . . . that either (a) a very substantial sum of money be obtained to erect a new building, to be known as the New England Academy of Medicine, which would house not only the Academy but also the Boston Medical Library and the Massachusetts Medical Society, including the *New England Journal of Medicine*, or (b) a substantial sum of money be obtained . . . to make the necessary alterations in the Boston Medical Library to provide attractive modern facilities and adequate stacks, and to cover in part, through increased income, the additional expense incurred by increases in its staff; . . . that the financial support of the Boston Medical Library by the working libraries be increased, in view of the improvement in service rendered to them and of the opportunity to cut down on their annual expenditures.

Already, plans are made by a group of men, among whom representatives of our library are conspicuous, to explore every possibility and to devise and later attempt to execute a comprehensive, broadly conceived plan for the future. As a Nation, we are literally in a death struggle with an implacable, relentless and powerful foe whose purpose is to enslave us, and it is quite likely that many of us may say that this is no time to bother about matters that seem to have no relation to the struggle we are making to win the war. Surely on further thought, however, every man of us will realize that this is the time of all others when we must guard and hold fast that which is good and has been amply proved to be a source of strength and inspiration.

DAVID CHEEVER, *President*

REPORT OF THE LIBRARIAN FOR THE YEAR 1941*

THE year 1941 saw the Boston Medical Library pass from a period of national emergency to one of war. Libraries pass through wars, except when destroyed, as some of our sister institutions in Great Britain and elsewhere were, less affected than many of our national foundations. Our stock in trade, books, still retain their influence even if uprooted and transferred to other quarters. Certain of our most valuable possessions have been moved to places of comparative safety, where they are still available but not so prominently displayed. The very moving has been helpful in recounting our treasures and will probably lead to a recataloguing of our most valuable books. Our incunabula in the Bullard Collection were last catalogued in 1929. Since that date, this one group of books has tripled in size, and to them have been added others in the Hyams Collection. Our manuscripts have also grown in number, and it now seems fitting to print a new list of all the manuscripts and books in the library known to have been issued before 1500. Such a volume is indeed contemplated. Fortunately, too, this year will see the completion of fifty years of service to the Boston Medical Library by Mr. James F. Ballard, whose knowledge of these books is outstanding. To him must fall the work of compiling the catalogue, but to the fellows and friends of the Library comes the opportunity to honor a man devoted to our interests.

The war has brought, as might be expected, certain changes in our library life. All foreign periodicals, except those coming from Great Britain and Russia, are now frozen in their respective countries. In some instances, before the mails closed down entirely, arrangements were made to hold periodicals for future delivery. Except for a few issues, presumably lost in transit, English periodicals are received regularly. During the year, large shipments of medical magazines were received from Russia by exchange for duplicate American journals. In view of the lack of foreign journals, the usual gifts for their purchase from the local medical societies were not solicited during the year. However, gifts for periodicals were generously donated by the New England Pediatric Society and the Greater Boston Medical Society.

The national emergency also closed, on June 30, our two projects of the Works Progress Administration. Much, however, had been accomplished, particularly in sorting and classifying our theses and in putting our catalogue in shape. The *Union Catalogue*, fortunately, was practically completed, except for typing of the cards. This additional portion, essential to make the catalogue useful, awaits only additional funds. Although the projects have stopped, we can regard the work done as a definite contribution of considerable value to the Library. One of the aspects, moreover, is being carried on to completion. The Boston Medical Library catalogue cards are being copied, as agreed, for the library of the Harvard Medical School. This is about half finished. The proposed binding project, also to be under the Works Progress Administration, was never begun. Certain binding apparatus, purchased in anticipation

*Presented at the annual meeting of the Boston Medical Library on March 3, 1942.

of the project, is a valuable accession to the Library. It is always salable, but will be held for the time being.

The war, also, has caused a change in our hours of opening and closing the Library, owing to a curtailment of oil used for heating. The hours were greatly restricted at one time, along with those of our tenants and our neighbor, who buys heat from us. Later in the year, we were able to lessen the restriction on hours, and at the present time we are open for a normal period.

Attendance and circulation have been maintained at approximately the same level as in 1940. The circulation, as was noted last year, is 25 per cent greater than it was in 1939. Ten thousand more books, pamphlets and bound or current journals are thus handled each year by our small staff, a heavy drain on their energies and good nature. In addition, our interlibrary loans have jumped from 219 items to sixty-two libraries in 1939 to 633 items to one hundred and twenty libraries in 1941. The assembling, the packaging, the arrangements for fees and their collection, the answering of correspondence and the supervision of these loans are a not inconsiderable added burden on the reference librarian. If the call for books, moreover, both by our readers and by loan, is kept up as the years go by, we shall be faced with an even more acute problem than we have known about for years. Our staff is too small to give adequate service.

In 1941, we added 2432 volumes to our store of books, somewhat less than in previous years. This is largely due to the decrease in volumes of periodical literature received owing to war conditions: only 582 volumes in 1941 as compared with 1995 volumes in 1939. The number of books acquired has actually increased from 1432 to 1824. Thus, our library grows in both stature and usefulness each year, but at the same time the labors of our staff are increasing. If we seem a little "short," we are just trying to put quarts into pints, or as Osler would say, we are driven from Dan to Beersheba.

A number of papers have been published by the staff, directly related to the Library. The director issued his annual report, "The Medical Books of 1940," in the *Bulletin of the Medical Library Association* for June. The Librarian's "Report for 1940" was printed in the *New England Journal of Medicine* for May 22, and he also published two historical papers based on our collections, "The War of 1812 and the Marine Hospital for the Port of Boston," in the *Bulletin of the History of Medicine* for June, and "The Problem of the Three Edward Warrens," in the *New England Journal of Medicine* for June 19. The death of Sir D'Arcy Power on May 18, an old friend of the Library, and indeed of all medical libraries and historians, was noted in an exhibit of books, pamphlets, pictures and letters in the rotunda and an obituary in the *New England Journal of Medicine* for July 3.

The Book Review Department, thanks to the generosity of the *New England Journal of Medicine* and our fellows and friends who review the books, continues to function in a satisfactory manner.

In the last year, the cataloguing of the Storer Collection of Medals has been brought up to date, listing all the accessions since the late Dr. Malcolm Storer issued his catalogue of the whole collection in 1931. Valuable additions have been made in the last few years, particularly the twenty-nine large plaques designed by Pierre Jean David (1789-1856), usually called David d'Angers. This French sculptor worked in Paris at the beginning of the nineteenth century. Many famous men and women sat for him. A nearly complete collection, originals and copies, is in the Musée David at Angers. Of particular interest is his monument to Gutenberg at Strasbourg. The medallions in our collection are of contemporary physicians, many of them well known in the history of medicine.

In 1941, our special collections were increased by modest accessions, largely through purchase by funds set up for the purpose. We have added twoscore incunabula to our growing list, now widely recognized as a group of books of national importance and becoming more widely used each year by scholars. American, English, Spanish and other imprints have been acquired, helping to round out our collection in fields of particular interest.

Of all the book auctions and sales that occurred in 1941, two have particular interest for us. On three days in June, the library of Sir D'Arcy Power was sold at auction by Sotheby and Company, of London. We received only four items out of twoscore bid for by cable. The prices in general were well maintained, some of the items selling for high figures. We obtained a good copy of the 1585 edition of Clowes's, *A Briefe and Necessarie Treatise . . .*, and the first collected (1639) edition of John Woodall's *The Surgeons Mate. . . .*

Another and still more unusual sale occurred at Gimbel Brothers in New York City on October 27. Many of the books offered were sold before the sale actually opened, and fortunately we had arranged with a New York dealer to purchase four books for us. The most significant was the *Prognosticon* (1483) of Dominicus Maria de Novaria, the only copy in America. The books were offered at bargain prices marked with sums such as $197.50. It seems unlikely that incunabula have ever been sold in a department store before.

The collection was part of the books assembled by O. H. F. Vollbehr, another section having been previously disposed of to the Library of Congress.

As usual, there have been special donations to the Library in 1941. One of the most important is the watch formerly owned by Dr. Amos Holbrook, of Milton, the vaccinator, and his honorary diploma of 1814 from the Massachusetts Medical Society.

In previous years, the Librarian has pointed out a course for the future growth of the Library and its sister institutions. Plans must be held in abeyance in wartime, but this does not mean that such plans should be abandoned. The whole library situation in Boston still presents the same problem and will do so even more acutely after the completion of the war. It is well to retain in mind the basic principle of a central reference library, with working units in various medical schools and hospitals. Only on such a broad foundation can the problem be solved. In this solution, the Boston Medical Library should ever retain a vital interest.

HENRY R. VIETS, *Librarian*

UNRECOGNIZED TYPHOID CHOLECYSTITIS AS A SOURCE OF HOSPITAL INFECTIONS*

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ACUTE infection of the gall bladder complicating the course of typhoid fever has frequently been noted since the report of Gilbert and Girode[1] in 1890. Similarly, the chronic cholecystitis associated with the typhoid-carrier state has been definitely established as a clinical entity. Thus, although the predilection of the typhoid bacillus for the gall bladder has been sufficiently emphasized, a diagnosis of chronic cholecystitis is usually made without the realization that in a definite number of these cases *Eberthella typhosa* may be the etiologic agent. When such patients are admitted to surgical wards for operative procedures, hospital personnel are exposed to unrecognized typhoid carriers for varying intervals of time. Similarly, in rare cases, acute cholecystitis complicating typhoid fever may also find its way into hospitals without recognition of the basic etiology. The recent epidemiologic investigation of two such hospital infections is considered of sufficient interest to merit discussion.

CASE REPORTS

CASE 1. Dr. R. S., a 25-year-old married house officer, was admitted to the medical service of his own hospital on December 16, 1941, with complaints of malaise, generalized pains and aches, and fever. He had been perfectly well until 3 days prior to admission, when he had noticed that he tired easily. The temperature at this time was normal. In 24 hours, the patient became aware of generalized pains and aches associated with slight soreness of the throat. On the following day, when it was found that the temperature was elevated, he was admitted to the hospital. On admission, physical examination was essentially negative except for diffuse redness of the throat.

Examination of the blood showed a red-cell count of 5,700,000 with a hemoglobin of 96 per cent, and white-cell counts varying from 3500 to 7300; the blood smear showed 69 per cent neutrophils, 20 per cent lymphocytes, 10 per cent mononuclears and 1 per cent eosinophils. Urinalysis was negative. The blood serum agglutination reactions against typhoid fever showed a gradual rise in titer from + in a dilution of 1:40 on December 17 to ++ in 1:320 on January 6. A blood sample submitted for a Widal test to the State Laboratory was reported positive on December 30. A stool culture was positive for *E. typhosa*.

The temperature remained elevated for about 10 days. The course was mild and uneventful except for an attack of acute right-upper-quadrant pain on December 25. The pain was severe and radiated to the right back and side, and was relieved only after the administration of morphine. The attack was associated with spasm over the region of the gall bladder. Tenderness in the right upper quadrant persisted for 5 days. The temperature became normal on the 11th hospital day. There was no recurrence of gall-bladder symptoms. The diagnosis was typhoid fever.

Epidemiologic investigation. To establish a source of infection, attention was directed first of all to the familial contacts of the patient. There was, however, no history of previous typhoid fever among the several members of his own family or that of his wife. Laboratory study of these contacts was entirely negative. The presence of a recent case of typhoid fever on the medical wards of the same hospital was then considered as a possible source of infection. The house officer denied any contact with this case. There was a history of at least two meals away from either his home or the hospital in the month prior to infection. Since no other cases had been associated with the restaurants named, this did not seem an important clue. The possibility of a missed case of typhoid fever was then considered as a source. The patient could, however, recall no recent case of either unexplained fever or peritonitis of unknown etiology. Inquiry was then made regarding patients with gall-bladder disease treated on his wards within the 4 weeks preceding onset. The records revealed 4 such cases during that time. The house officer was particularly aware of 1 patient, Mrs. R. G., who had had an operation for chronic

*This investigation was conducted in co-operation with the Boston Health Department.

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cholecystitis and who subsequently had a second operation for stone in the common duct. There was persistent bile drainage following both operations. The house officer had frequently changed the dressings of this patient. In addition, he had helped prepare "cocktails" for her made from her own bile. The admission and discharge dates in this and in the 3 other recently operated gall-bladder cases were obtained. Visits were then made to the homes of these persons, and blood and stool specimens were obtained. Two of these 4 patients gave a past history of typhoid fever. One of these was Mrs. R. G., who had had the disease about 40 years previously. The Widal test and stool culture of specimens from this patient were both positive for *E. typhosa*. Stools in the remaining 3 cases were negative.

Source case. Mrs. R. G., a 48-year-old woman, was admitted to the surgical ward on October 20, 1941, with a chief complaint of recurrent upper abdominal pain and jaundice. Her first attack occurred 20 years previously, and was followed by several such episodes for about a year. The patient was then asymptomatic until about a year prior to admission, when there was sudden onset of jaundice followed in 24 hours by severe cramp-like pain in the upper epigastrium radiating posteriorly to the interscapular region. There were several subsequent attacks, which came on approximately once a month until 4 months before admission. One month prior to entry, attacks began to occur once each week, the last being 17 days before admission. X-ray studies performed by the patient's physician revealed gallstones.

Physical examination showed a slightly jaundiced middle-aged woman in no apparent distress. The only significant physical finding was a minor degree of jaundice of the skin and scleras. Examination of the blood showed a red-cell count of 4,550,000 with a hemoglobin of 90 per cent, and a white-cell count of 4500; the blood smear showed 59 per cent neutrophils, 32 per cent lymphocytes, 3 per cent mononuclears, 4 per cent eosinophils and 2 per cent basophils. The bleeding time was 3½ minutes, the clotting time 5¾ minutes, and the prothrombin time 13.5 seconds. The icteric index was 18. Urinalysis was negative except for an occasional slight trace of albumin. The hospital diagnosis was chronic cholecystitis with cholelithiasis.

On October 22, the patient underwent cholecystectomy. Many stones were found in the common duct. Postoperative cholangiograms confirmed the operator's impression of residual common-duct obstruction. The stools were clay colored at several examinations. There was drainage of about 4 cc. of bile daily.

The patient's condition remained unchanged until November 22, when a second operation was performed, and the common duct was re-explored. Many stones were removed. Following the second operation, there was a large amount of biliary drainage through a T tube and through the wound. The biliary drainage through the T tube persisted throughout the hospital stay and continued even after discharge. Cholangiograms following the second operation suggested a stone in the terminal portion of the common duct. The patient was discharged on December 12, 1941.

Case 2. Miss M. C., a 22-year-old affiliated student nurse, was admitted to the medical ward on January 2, 1942, with complaints of headaches, chills, nausea and vomiting. She had been well until 2 days before admission, when she developed a headache and began having chilly sensations. Later that day, she became nauseated and vomited watery material. The next day, the headache persisted. The patient complained of backache. Although she was still nauseated, there were no other gastrointestinal complaints. The past history was not important except that the patient had received a course of antityphoid inoculations early in her training course, approximately 2 years and 2 months prior to the onset of this illness.

On admission, the temperature was 101°F., and the pulse 90. Physical examination was negative except for slight redness of the throat and harsh breath sounds, with scattered coarse rhonchi over both lung fields.

The white-cell counts varied from 6400 to 3900. The hemoglobin was 85 per cent, and the smear showed 74 per cent neutrophils and 26 per cent lymphocytes. Urinalysis was negative. Blood culture on January 4 was positive for *E. typhosa*. A positive Widal reaction in a dilution of 1:160 was reported on January 8. The temperature was elevated until January 15. The course was mild, and the patient made an uneventful recovery. The diagnosis was typhoid fever.

Epidemiologic investigation. The epidemiologic investigation of this case revealed that the patient had worked, during the 4 weeks preceding the onset of her illness, on a single surgical ward. Inquiry was then made concerning possible missed cases of typhoid fever or surgical cases that might have been of typhoid origin. This brought up for consideration 3 patients with gall-bladder disease who had recently been treated on that ward. All 3 had been discharged, and home visits were made to establish a possible typhoid etiology. One, Mrs. S. R., a 28-year-old housewife, who had undergone cholecystectomy on December 7 following a diagnosis of acute cholecystitis, had a positive Widal reaction on January 21. She had been discharged from the hospital on December 27. A stool culture from this patient, taken on January 21, about 6 weeks following operation, was positive for *E. typhosa*. However, the history did not disclose a previous attack of typhoid fever. This, in addition to the fact that she was only 28 years old, made it appear unlikely that the patient was a typhoid carrier. A careful review of her recent hospital admission revealed an acute febrile illness, with symptomatology and a white-cell count compatible with the diagnosis of typhoid fever complicated by acute cholecystitis. The student nurse had frequently changed the surgical dressings of this patient following her operation. The discovery of this previously unrecognized case of typhoid fever necessitated the search for the ultimate source of infection among the contacts of the newly discovered case. One such contact, her 64-year-old mother-in-law, gave a history of typhoid fever 25 years previously. For several years, the mother-in-law had had recurrent attacks of right-upper-quadrant pain, together with other symptoms usually associated with chronic disease of the gall bladder. It was also learned that 5 years previously, while she was visiting the family of a daughter residing in Canada, her son-in-law had developed typhoid fever. Laboratory study of this suspect revealed that she was a chronic typhoid carrier and was, therefore, the source of infection for Mrs. S. R., who in turn infected the student nurse.

Source case. Mrs. S. R., a 28-year-old housewife, was admitted on December 6 with a chief complaint of right-upper-quadrant pain of 1 day's duration. About 3 weeks before admission, a severe upper respiratory infection, associated with "heaviness of the chest" and productive cough, appeared. About a week later, the patient noticed that she tired more easily than usual. Her arms and

legs felt heavy. She could scarcely "stand on her legs." After this feeling of tiredness had persisted for about a week, she found her temperature to be 104°F. She consulted a physician, who advised bed rest. The fever persisted. On December 1, she became aware of a dull ache in the right upper quadrant. This subsided until 24 hours prior to admission, when the pain returned with increasing severity. It was intense and colicky, and radiated to the back. She became nauseated and vomited several times. There was no jaundice or clay-colored stools. The past history revealed an attack of right-upper-quadrant pain 1 year previously that had lasted for 3 days.

On admission, the temperature was 103.4°F., and the pulse 120. Physical examination revealed an alert, feverish, restless woman in obvious distress. General examination was otherwise negative except for spasm and tenderness in the right upper quadrant. Examination of the blood showed a white-cell count of 8050, a red-cell count of 4,130,000 and hemoglobin of 70 per cent. Urinalysis was negative. The icteric index was 11.

On December 7, the gall bladder was removed under spinal anesthesia. It was tense, edematous and inflamed, with several small areas of necrosis. No stones were found.

Following operation, the patient ran a spiking temperature. On December 9, 2 days after operation, the white-cell count was 9000. The temperature on that day was 101.4°F. The temperature gradually subsided and was normal on December 24. Except for the temperature, the course was uneventful, and the patient was discharged on December 27. The hospital diagnosis was acute cholecystitis.

Discussion

The epidemiologic investigation in Case 1 revealed that a house officer on a surgical ward developed typhoid fever following contact with a patient with chronic cholecystitis who was subsequently found to be a typhoid carrier. Investigation of Case 2 showed that a student nurse on a surgical floor in another hospital had developed the disease while taking care of a recently operated case of acute cholecystitis, which was found actually to be typhoid fever manifested by acute cholecystitis. The symptoms associated with the acute gall-bladder attack distracted attention from the basic disease, typhoid fever. The occurrence of acute cholecystitis as the outstanding feature of typhoid fever has been reported in the literature.[2] It has also been shown that acute involvement of the gall bladder, which is occasionally associated with typhoid fever, may progress to perforation.[3]

It has been demonstrated that stool cultures submitted by typhoid carriers subsequent to cholecystectomy become negative in most cases within a few days to three weeks after operation.[4] However, the stool culture may remain positive for a much longer time and may eventually become negative. In the source case, Mrs. R. G., a positive stool was obtained as late as seven weeks after the second operation. All subsequent cultures of the stools and bile, including those grown in an enrichment medium, have been negative. Thus, the evidence indicates that the carrier condition in this case has been cured.

It is difficult to say whether or not the stool culture obtained from the second source case, Mrs. S. R., will continue to be positive. Since the gall bladder has been removed, it is very likely that she will become noninfectious in a short time. One wonders whether she might have become a carrier if the operation had not been performed. Garbat[5] showed a high incidence of carriers among patients with typhoid fever who manifested symptoms of cholecystitis either as a complication during the disease or as a sequel during convalescence.

It is an interesting coincidence that a similar mode of infection should have been demonstrated in 2 cases of typhoid occurring within a few weeks of each other in two different hospitals. This raises the question of how often typhoid bacilli are associated with chronic disease of the gall bladder. Isolated reports demonstrating this relation are not infrequent. In 1941, Botsford[6] reported a patient with suppurative cholecystitis who, on admission to the hospital, was found to be a chronic typhoid carrier. Too much reliance cannot be placed on older studies that attempted to demonstrate the frequency with which typhoid bacilli occurred in chronic disease of the gall bladder. It is to be expected that improved bacteriologic technics will be more successful in culturing this organism. More recently, Dickinson[7] stated that in a study of the bile of patients coming to operation for gall-bladder disease it was found that 10 per cent are of typhoid origin. A similar study is now being carried on by the Massachusetts Department of Public Health.

It has been demonstrated that cholelithiasis frequently accompanies chronic gall-bladder disease of typhoid origin. Garbat[5] reported in 1922 that stones were found in 3 out of 21 cases that went to operation. Förster,[8] in an analysis of several hundred carriers, found the same proportion of gallstone sufferers. However, criteria for the carrier state are more rigid today than they were twenty or thirty years ago. Many patients formerly classed as carriers are now considered convalescent typhoid cases. Thus, Bigelow and Anderson,[9] in 1933, noted that, in 12 carriers coming to operation, stones were found in all. The question of the cause of stone formation in typhoid gall-bladder carriers is beyond the scope of this paper. However, the symptoms associated with the presence of gallstones often serve as a valuable lead to the epidemiologist attempting to seek out a source of infection among the contacts to a case of typhoid fever.

The protection of hospital personnel against typhoid fever is a problem that deserves consid-

erable attention. The unrecognized case of typhoid cholecystitis is not the only form of surgical typhoid that finds its way into hospitals without a realization of the typhoid etiology. Typhoid fever is protean in its clinical manifestation. At present levels of incidence, typical cases are uncommon. Of those reported, many are decidedly unusual in their clinical manifestations, and as a result, a patient may be hospitalized for many days before a diagnosis is made and proper precautions instituted to prevent secondary cases.

For many years, it has been a recommended procedure in hospitals to inoculate members of their personnel, including physicians, nurses, laboratory workers and ward attendants, against typhoid fever. In addition to the primary series of three injections, a stimulating dose of 0.5 cc. must be administered each year to maintain a sufficient degree of immunity. Recent reports from the Army Medical School[10] indicate that 0.1 cc. of typhoid vaccine, given intradermally as the stimulating dose, offers an excellent level of immunity. The intracutaneous route eliminates practically all the constitutional reactions. The intradermal method has also been advocated by some[11] as the method of choice for primary inoculation. However, all observers[12] are not in accord concerning the superiority of the intradermal route. It is still generally recommended that the initial series of three injections be given subcutaneously.

In Case 2, the patient had received the initial series of typhoid inoculations two years and two months previous to the onset of the disease. The stimulating dose had not been administered. One wonders whether the mildness of the clinical course may have been the result of previous immunization.

The house officer, Case 1, had never received antityphoid inoculations. It is apparent that many interns in Massachusetts hospitals do not receive the protection afforded by typhoid vaccination. Whereas immunizing procedures for nurses are often carefully supervised, house officers are left to shift for themselves in this respect. When schedules are drawn up to immunize hospital personnel, it is essential that house officers be included.

In the management of gall-bladder cases on hospital wards, attention must be given to the possibility that a definite number may be of typhoid origin. The practicability of routine stool cultures on all such cases has not yet been definitely established. Further studies, utilizing modern cultural methods, will demonstrate what yield may be expected by this method of attack. The possibility of employing the Widal reaction as a screen merits further investigation. According to this procedure, stool cultures would be submitted only by patients who show some reaction in the Widal test. At present, a practical approach is to establish in every case of gall-bladder disease whether there is a history of typhoid fever or of an unexplained fever consistent with this disease. Whenever a case of chronic cholecystitis presents a past history of typhoid fever, the patient should be kept on precautions until laboratory studies exclude the carrier condition. When such cases are admitted to hospitals for elective surgery, it is preferable that the laboratory work be done prior to hospital admission. In many cases, it will be found that the history of typhoid fever dates back many years. Such an interval does not exclude a carrier condition, since it has been shown that the carrier state may exist for an indefinite number of years until cured by operation.[13] Since a fair proportion of chronic carriers do not present a past history of typhoid fever, extreme care should be exercised by all persons handling dressings and discharges from all gall-bladder cases. Hospital personnel in charge of these cases must constantly bear in mind that a certain proportion of all cases of chronic cholecystitis are of typhoid origin.

Summary

Two cases of typhoid fever that occurred among the personnel on the surgical wards of two different hospitals are presented. The epidemiologic investigation of the first case revealed a previously unrecognized typhoid carrier as the source of infection. The carrier had been admitted for operation with a diagnosis of chronic cholecystitis and cholelithiasis. The epidemiologic investigation of the second case revealed as the source of infection a missed case of typhoid fever admitted to the hospital for a complicating acute cholecystitis; this primary case was in turn traced to a chronic carrier, the ultimate source.

Protection of hospital personnel by routine antityphoid inoculation is an essential preventive measure in all hospitals.

When cases with gall-bladder disease are admitted to hospitals for operative procedures, careful histories should be obtained regarding previous typhoid fever. In cases presenting such a history, laboratory studies should be instituted to rule out the typhoid-carrier state.

The possibility of typhoid etiology should be considered in all cases of chronic cholecystitis. Acute cholecystitis may in rare cases be the most outstanding clinical manifestation of typhoid fever.

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MEDICAL PROGRESS

ALLERGY: SERUM REACTIONS, WITH PARTICULAR REFERENCE TO THE PREVENTION AND TREATMENT OF TETANUS*

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INSTRUCTIONS in first aid often include directions that every victim who sustains a punctured wound receive immediately a dose of tetanus antitoxin — advice that is entirely proper provided that it is not definitely known that the patient is adequately protected by previous doses of tetanus toxoid. Unfortunately, however, the instructions do not always include a warning of the reactions that may occur immediately in a few cases or later in many cases; nor do they always include directions for the precautions that should be taken in each case. In the excitement of the moment, it is hard to realize the possibility that the effects of the serum treatment may be even worse than those of the disease that the antitoxin is supposed to prevent. It is possible for the serum to kill the victim in a matter of minutes, and it is not only possible but probable that a delayed serum reaction will occur in from five to fifteen days after the dose has been administered. I am quite aware, however, that, without serum, tetanus may occur and that any measure that will prevent its development should be applied. Zinsser, Enders and Fothergill[1] quote the figures of Robertson[2]: before 1903, when the American Medical Association publicized the prophylactic use of tetanus antitoxin, tetanus had developed in about 10 per cent of Fourth of July injuries, and the mortality was almost 100 per cent. By 1914, however, the use of prophylactic antitoxin had reduced the incidence to 0.2 per cent: there were only 3 cases in 1506 injuries. Statistics in the British Army also showed striking evidence of the prophylactic value of tetanus antitoxin. Figures for the incidence of tetanus in modern wars are given in a very instructive table in a recent paper by Hall[3] and are reviewed below. I have only one significant point to make: whenever one administers serum, it should be done intelligently and with full appreciation of the possible consequences.

Reactions following the administration of foreign proteins are of several types. Some occur in persons who are normal except that they have previously been treated with serums of the same kind; such patients may be actively sensitized, and may react to a second dose with the same immediate anaphylactic shock that kills the sensitized guinea pig. Other reactions, which occur in normal persons even without previous treatment, vary widely in their time of onset as well as in their characteristics. They are varieties of serum disease, which, after all, is a normal response. Finally, immediate reactions, either local or general, may occur in persons who are naturally "allergic" or sensitive to the foreign serum. These three types may overlap and occur together in certain cases.

REACTIONS TO FOREIGN SERUM

Anaphylactic Reactions

True anaphylactic reactions may be fatal. The guinea pig is sensitized with ease. The rat is sensitized with great difficulty. It is very fortunate that man is hard to sensitize. So far as anaphylaxis is concerned, he is much more like the rat than like the guinea pig. Nevertheless, there are reports that indicate that man can be sensitized artificially by previous doses of foreign serum.

In 1931, I[4] collected the reports of a series of 19 cases of true anaphylaxis in man. Each of the patients had received a first dose of serum, usually in the form of diphtheria antitoxin, without symptoms of any kind, and then, after an interval that was sometimes as short as ten days, and in other

Reprints of articles in this series are not available for distribution, but the articles will be published in book form. The current volume is *Medical Progress: Annual, 1940* (Springfield, Illinois: Charles C Thomas Company, 1941. $4.00).

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cases as long as two years, the second dose was given and was followed within a few minutes by a severe and fatal reaction. The outlines of the individual case histories were included in this report, and the variations in the types of cases, particularly in the time relations involved, were discussed at some length. In 1932, Waldbott[5] published a study of 9 fatal cases of the same sort, 7 of which were typical of anaphylactic shock; the other 2 occurred in patients who were allergic.

Perhaps these reports did some good. The fact is that since 1932 the literature has contained very few reports of fatal anaphylaxis in man, the criteria being: no reaction whatever to the first dose; an interval of time; and immediate death after the second dose. Anaphylaxis can occur in man, but the cases are rare.

Lord and Heffron[6] noted three deaths in 1755 patients treated with antipneumococcus serum. One of them was a man who had been given 57 cc. of serum during treatment for pneumonia. Empyema developed; the fever persisted; and on the twenty-third day it was decided to give serum again. After only 2 cc. had been injected, the patient died.

Surgeons should recognize the fact that ether anesthesia is not a protection against anaphylactic shock. Quill[7] has reported the case of a Negro who was given tetanus antitoxin during an operation for gunshot wound and who died in three minutes.

The Arthus phenomenon is a local necrosis produced typically in rabbits by repeated injections of foreign serum. Gougerot and Blum[8] report a patient who, three years after a prophylactic dose of tetanus antitoxin, was given it again. Within five minutes, nausea and generalized pains occurred. In six hours, the patient was covered with urticaria and had edema of the glottis. In forty-eight hours, a marked necrosis developed at the site of the serum injection.

Actual figures for the incidence of true anaphylaxis in man are not known. Most authors write of "reactions" after doses of serum and do not always indicate whether the patient was treated previously or whether he was hypersensitive. The incidences of serum reactions of all kinds are therefore discussed together below. Meanwhile, it is proper to ask whether every patient treated with a foreign serum becomes clinically sensitive to that serum. And if not, how often does sensitiveness occur? How real is the danger? The questions are difficult to answer, and for at least two reasons: the real test requires the deliberate injection of serum, which, if the person is sensitive, might well produce a severe reaction and would be dangerous; and studies of skin tests with the serum are difficult to interpret. In other allergic states, — hay fever, for example, — it is known that skin tests are not always a direct measure of clinical sensitiveness and that the reaction of the skin is not always parallel in size to the reaction of deeper tissues; however, skin tests are helpful.

In 1924, Hooker[9] performed skin tests with horse serum on a series of students and nurses before and after immunization with diphtheria toxin-antitoxin mixtures. At the start, 59 of the total of 367 persons, or 16 per cent, reacted positively, and of these, only 23, or less than half, had had serum previously. After the course of injections, 100 of those subjects whose first tests were negative were studied again. Twenty-eight (28 per cent) gave immediate reactions, and 38 (38 per cent) gave delayed positive reactions. These results refer only to the skin test. However, Hooker's assumption that a "parallelism between skin reactions and general hypersensitiveness is reasonable" has some support.

In 1929, Gordon and Creswell[10] observed that since diphtheria toxin-antitoxin had come into general use, the incidence of serum reactions of all kinds had increased. Of 556 persons who had been previously immunized and were injected with serum, 74.1 per cent developed serum reactions, whereas in 1750 controls without treatment, the incidence of reactions was only 16 per cent. These figures indicate that the immunization has a generalized effect.

Tuft,[11] in 1932, repeated Hooker's experiment. After the toxin-antitoxin injection, he found that positive skin tests ("moderate" and "marked") occurred in about 19 per cent of 227 treated patients, as compared with only 1 per cent of the 100 control subjects. Eye tests were positive in 8 per cent of 148 treated patients, and in only 1 per cent of 100 controls. Antibodies were demonstrable in a number of those treated, "reagins" (passive transfer bodies) in 20 per cent, and antistreptococcus hemolysins and agglutinins (heterophil antibodies) in 25 per cent and in 39 per cent, respectively. This is further evidence that the sensitiveness is generalized and not merely a skin phenomenon.

Evidently, then, the production of active sensitization is not uncommon, even when the sensitizing dose is extremely small. The point is that before administration of serum to a new patient, it may be of considerable practical value to know whether or not serum has been given before.

Serum Disease

Serum disease occurs in normal persons. The symptom complex presumably is produced by a poison liberated by the interaction between the diminishing amounts of foreign (horse) serum

still remaining in the circulation after the injection and the increasing amount of antibody that the organism develops. When the two factors come into a certain relation with one another, serum disease occurs. In most of the cases, serum disease begins between the seventh and fourteenth days and usually lasts from two to seven days. Sometimes, however, the onset is earlier than this, — on the sixth day or on the fourth day, or even on the second day, — when it is referred to as an "accelerated" reaction. When it occurs during the first day, or perhaps during the first hour, it produces a clinical picture that is quite the same as that in the anaphylactic reaction described above. The point to observe is that there is no sharp clinical boundary between the normal response — serum disease — and the more rapid and violent reaction, or anaphylaxis.

The symptoms of serum disease are well known. Urticaria and joint pains, which are the commonest, depend on a sudden edema of the skin or of the joint structures. Edema may also develop in nerves and thus produce neuritis, as reported by Hoagland,[12] Brahdy[13] and Bennett.[14] Lemierre's[15] patient developed cerebral symptoms, with loss of consciousness and aphasia. Clog[16] described several patients who developed abdominal pains severe enough to indicate operation for "appendicitis." Swelling of the mesenteric lymph nodes and hyperemia of the peritoneum were found.

The difference between the two types of response depends on the degree of individual reactivity. In anaphylaxis, the first dose stimulates the production of antibodies, which then persist in the blood or tissues or perhaps in both, instead of disappearing slowly as they do in most cases. In serum disease, antibodies develop slowly during the incubation period and reach their maximum immediately after the clinical symptoms have disappeared. They are often in high concentration and can be demonstrated in various ways — by the skin tests, by the precipitin reactions and by injection of the patient's serum into the skin of a normal person and subsequent tests of the prepared site (this is the so-called "Prausnitz–Küstner reaction"); or the patient's serum can be used to transfer sensitiveness to a guinea pig. This easy demonstration by various methods is quite different from what one obtains in the naturally sensitive person described below.

These laboratory findings easily explain why it is so very dangerous to administer a second dose of serum shortly after the occurrence of a serum disease. The high degree of sensitiveness of these patients is not so very surprising. Freedman[17] reports a typical case, in which a six-year-old boy received a dose of diphtheria antitoxin and ten days later developed serum disease — almost as expected. Twenty days after that, he was tested at the clinic for his sensitivity by intracutaneous injection of a dose of 0.05 cc. of horse serum. Within two minutes, he developed a generalized urticaria and then severe asthma. In spite of heroic doses of adrenalin and treatment in a Drinker respirator, he died in about eight minutes.

Blotner[18] describes a twenty-two-year-old man who had been given a dose of tetanus antitoxin three years before receiving 1500 units of the same antitoxin intramuscularly. There was no immediate response, but eighty minutes later the patient developed a generalized itching with a rash. Adrenalin was given at frequent intervals, at first subcutaneously and later intravenously. He became cold and clammy. The blood pressure fell to 80 systolic, 40 diastolic. In five hours, the patient was taken to the hospital in an ambulance, where fluids were administered in large quantities, and he recovered. This was an accelerated reaction due to the preliminary treatment.

Ferguson[19] reports the case of a six-year-old boy who was injured by an automobile and was given three minims of tetanus antitoxin, followed by a complex barbiturate drug (Evipal) intravenously. He went to sleep but in fifteen minutes suddenly had trouble with his breathing. Twenty-five minutes later, a large wheal appeared at the site of the antitoxin injection and spread all over the arm. Another complex drug (Coramine) was administered, with little benefit. The injection of 5 per cent glucose in saline solution intravenously helped at first so that in two and a half hours the patient was transferred to the hospital ward. An hour later, however, he suddenly stopped breathing. Death was considered to be due to anaphylaxis, but I wonder whether the drugs may not have played a major part. At autopsy, the trachea and bronchi were filled with frothy sanguineous material, and almost all the two lower lobes showed hemorrhagic consolidation.

Allergic Reactions

Allergic reactions occur only in persons who have a certain taint (probably inherited) that gives them a special capacity to develop sensitiveness. They appear to be "naturally sensitive." They usually give a past or familial history of eczema, hay fever or asthma. This is the important group, for serious and sometimes fatal reactions can follow what appears to be the first dose of serum. There may be no history of previous contact with the same foreign substance. The reaction appears to come out of a clear sky except for the fact that further study often reveals the allergic background and the allergic constitution of the patient.

In 1931, I[4] reviewed the cases of several patients who died in a few minutes following a dose of serum that was evidently the first. Since that time, however, many accidents have been reported, but not many of them were fatal.

Incidence of serum reactions. How often do serum reactions occur? The literature has been reviewed by Tuft,[20] Zinsser et al.,[1] Harten and Walzer[21] and more recently, in a very comprehensive article, by Rutstein and his associates.[22] According to the last authors, immediate serum reactions can be grouped on a clinical basis into three definite classes. Thermal reactions (fever and chills) occurred as the only response in 218 patients, or 9 per cent of the total of 2340, treated with a concentrated, type-specific antipneumococcus horse serum by intravenous injection. Anaphylactic reactions, with itching, urticaria, asthma, angioneurotic and, sometimes, laryngeal edema, occurred in 5 per cent. Circulatory reactions, with a rapid, thready, irregular pulse, shock and, sometimes, vascular collapse, occurred in 3 per cent. And, finally, miscellaneous reactions — nausea, vomiting, headache, lumbar pain and dyspnea without asthma — occurred in 4 per cent. Combinations of these reactions were observed in another 10 per cent, to make a total of 32 per cent of the patients who developed reactions of one type or another. In another paper,[23] the same authors point out that reactions of all types are commoner with a history of asthma (45.5 per cent of 101 cases) than they are without such a history (29.6 per cent of 3114 cases). Obviously, the allergic background is always significant, and one should ask each time for evidences of allergy, such as hay fever, asthma and eczema, in the patient and in his family.

The incidence of serum reaction is shown by many figures in many papers. It is, however, not profitable to study them too closely or to attempt any direct comparison between the different reports. As Fox[24] says, variations in the proportion of reactions depend on many different factors: the degree of sensitiveness of the patient under treatment is one; his age is another. The particular lot of serum used may be a third factor. It is known, for example, that the serum from one particular horse may give a larger proportion of reactions than another lot of serum, and the commercial laboratories accordingly pool the serums from different animals. The route by which the serum is injected changes the figures. In the early days, when Park[25] reviewed the treatment of diphtheria by antitoxin, he found that death due to the serum had occurred in only 5 cases among a total of 350,000 children treated. In those days, the doses were of straight horse serum and were given subcutaneously in amounts varying from 5 to 15 cc.

The serum treatment of pneumonia is given by the intravenous route, and the incidence of serum disease depends on the quantity injected. Before methods of concentration were employed, this serum was given in quantities of 100 cc. or more, and delayed reactions (serum disease) occurred in at least 90 per cent of the cases. At present, practically all serums are concentrated. As a result, Lord and Heffron[6] have found the incidence of serum disease to be much lower: it occurred in only 20 per cent of 1423 patients recovered from pneumonia with serum treatment. When scarlet-fever antitoxin was used in crude form, serum disease occurred, according to Toomey and Baker,[26] in 38.5 per cent of 283 patients, but when concentrated antitoxin was employed, it developed in only 11 per cent of 524 patients.

Rabbit serum was first used by Horsfall and his associates[27, 28] at the hospital of the Rockefeller Institute as a treatment for pneumonia. In 1937, they treated 22 patients with doses varying from 32 to 268 cc. Twenty-one recovered from the pneumonia, and a mild serum disease developed in 12 (57 per cent). In 1938, the same authors, in a report on 67 cases of pneumonia treated with rabbit serum, observed that except in Type 3 pneumonia the mortality was as low as 3.7 per cent. Serum disease occurred in 40 per cent. This figure, however, was much less than that when horse serum was used in the same hospital. Unconcentrated horse serum produced serum disease in 95 per cent of 100 consecutive cases. Rabbit serum, therefore, not only appears to be better than horse serum as a conveyor of antibodies, but produces serum reactions much less frequently. It should be very useful for patients who need serum treatment and yet are sensitive to horse serum. Volini and Levitt[29] also used rabbit serum. They gave an average of 40 cc. of concentrated antipneumococcus rabbit serum intravenously to 153 patients and found serum reactions in 28 per cent. Wood[30] treated 50 pneumonia patients with quantities of immune rabbit serum varying from 10 to 150 cc. injected intravenously. He observed chills and fever reactions in from 26 to 50 per cent, and serum disease developed later in 41 per cent of these cases — an incidence similar to that noted by Horsfall et al.[27, 28] Meanwhile, one should note that it is not the quantity of total protein that is important: it is the specificity. Fox[24] found that pooled human convalescent serum used for the treatment of scarlet fever produced reactions in only 1 per cent of 420 patients.

Recently, Coghill and his associates[31] have described a method of "despeciating" serum by split-

ting off the carbohydrate complex with enzymes like takadiastase; they contend that the product retains about half its diphtheria antitoxin content, whereas it loses its capacity to sensitize guinea pigs to horse serum. Top and Watson[32] have treated 61 children with despeciated antitoxin. Although these patients were selected deliberately as a bad group presumably sensitive to horse serum, serum reactions occurred in only 10 per cent.

Reactions to Tetanus Antitoxin

Tetanus antitoxin causes reactions that are entirely similar to those after diphtheria antitoxin or antipneumococcus serum. Newell and McVea[33] have analyzed 500 patients who were given prophylactic doses of tetanus antitoxin; 59, or 11.8 per cent, developed some type of reaction. Local urticaria developed in every case at intervals varying from a few minutes to two days. Serum sickness, however, occurred in only 22 patients (4.4 per cent). This low figure is probably explained by the relatively small amount of horse serum injected. Schaeffer and Myers[34] treated a patient who had active tetanus and who was so sensitive to horse serum that even tiny doses could not be tolerated. Despeciated tetanus antitoxin was obtained and was injected in slowly increasing amounts, at first intracutaneously, then subcutaneously and finally intravenously. No reactions occurred, and later it was possible to give 10 cc. of the undiluted material intravenously and with no reaction. A total of 140 cc. was injected in various doses, and the patient recovered.

PREVENTION AND TREATMENT OF SERUM REACTIONS

The prevention and treatment of serum reactions are accomplished best by care in the selection of cases and in the administration of serum. Drugs have been tried, but no one of them is very successful. As a method of prevention, Lucchesi and Bowman[35] gave ephedrine and then combinations of ephedrine and calcium in regularly repeated doses to a group of patients; this regimen was begun at the time when the foreign serum was injected. The incidence of serum disease, however, was only slightly influenced, occurring in 38 per cent of the untreated group of patients and in 33 per cent of the treated group. Horsfall et al.[27,28] have recommended that acetylsalicylic acid (aspirin) be given by mouth just before or at the time of the serum injection, but they do not state the dose or present evidence that it does good.

After serum disease has developed, there is not very much that can be done about it. Furthermore, the effect of any treatment is hard to evaluate because the disease is not always long and one cannot be quite sure that the patient who does well with treatment may not also have done well without treatment. Stout and Kisotchek[36] gave hypertonic glucose to 10 patients with serum disease, with some relief. Foshay and Hagebusch[37] used histaminase, saying that 20 out of 22 unselected patients were relieved by the material, which was given sometimes by mouth, sometimes by intramuscular injection and sometimes by both methods together.

A very thorough presentation of the technical details of this subject, including general rules to be followed in the administration of therapeutic serums, is given in a special article prepared by Fantus and Feinberg[38] for the *Journal of the American Medical Association*. As soon as the principles are understood, these rules become almost obvious. Before any foreign serum is injected, it is essential to ask two questions. The first is, Have you ever had serum given to you before? The reason for the previous dose, the type of serum used and, especially, the presence or absence of serum disease after this earlier treatment are important details. The second question is, Are you allergic? That is, has the victim ever had hay fever, asthma or eczema, or has anyone in his family ever had one or another of these symptom complexes?

A test for serum sensitiveness should always be made. There are several methods. A scratch is made with a sharp needle or knife point through a drop of the serum. It should be controlled with a similar scratch through a drop of physiologic saline solution or of water. An intracutaneous test is much more delicate, but may give false-positive reactions unless the serum is diluted ten or even one hundred times with physiologic saline solution. Again, the test should always be controlled with similar injections of something else, such as egg white in a 1:100 dilution or ragweed extract in a 1:1000 dilution, but saline solution alone usually suffices—made with the same syringe beforehand or, better, with another perfectly clean syringe. With both the scratch and the intracutaneous methods, reactions appear in ten or fifteen minutes as typical urticarial wheals, with sharp advancing borders and surrounding erythema or redness. They should be interpreted with due regard for the control reactions.

One performs eye tests by applying a drop of the serum, diluted 1:10 with physiologic saline solution, directly to the conjunctival sac. When the serum is used undiluted, false-positive, irritative reactions may occur. If the patient is sensitive, the eye becomes red at once, and the reaction may include edema of the conjunctiva. It can be relieved promptly by the instillation of a drop of 1:1000 epinephrine (adrenalin) in watery solution.

The intravenous test for sensitiveness has been used by Loughlin, Spitz and Bennett[39] and by

Wood.[30] The former give a small dose (0.1 cc.) of the foreign serum diluted with 5.0 cc. of physiologic saline solution and inject it into the vein slowly. If, during the injection, the blood pressure falls 20 mm. or the pulse rate increases 20 beats, the patient is considered sensitive, and the injection is stopped. One or 2 minims of epinephrine can be injected intravenously through the same needle if severe reactions develop. Wood uses a larger dose, — 1.0 cc. of serum diluted with 20 cc. of saline solution, — and he waits a whole hour for reactions to develop before he proceeds with his therapeutic dose. Obviously, such tests in a highly sensitized patient may result in severe and even dangerous reactions.

The relative value of these different tests — indeed, the real value of any test as an accurate measure of the degree of sensitiveness — is far from clear. In hypersensitiveness, antibodies are attached to cells, and to some cells more than to others. The eye or the skin may be more sensitive, or it may be less sensitive than any other more vital tissues — the bronchial mucosa for example. In an unpublished study in our clinic, Rasch[40] found that the skin test (scratch method) gave good reactions to dilutions of ragweed-pollen extract four to eight times as weak as the lowest strength that reacted in the eye. Tuft[20] has stated that a positive eye test to horse serum never occurs in the absence of a positive skin reaction. Brown and Sechzer[41] compared intradermal and eye tests with rabbit serum in 101 patients in their allergy clinic; in both methods the 1:10 dilution was used. Only 1 patient gave a positive eye test, whereas 32 reacted positively to the intradermal injections, 1 of them being so sensitive that the test alone induced a generalized urticarial eruption. Toomey and August[42] found no fixed relation between the presence or absence of slightly positive skin tests at the time of serum treatment and the subsequent appearance of serum disease. Davis[43] has studied this further. In 200 patients (180 children and 20 adults) ill with diphtheria, she found positive skin tests in 39 per cent. Of those with negative skin tests (61 per cent of the total), 22.1 per cent developed a serum reaction after the administration of antitoxin, whereas of the 39 per cent who were skin sensitive, 28.2 per cent reacted later — the figure was higher, but not much higher.

On the whole, I believe that the history is the vital criterion, but that skin tests should be made as a check on the history. The finding of a positive reaction to horse serum constitutes a significant warning of a danger that is very real. A positive skin test may mean a general sensitivity, but not always, and if the skin reaction is not large it may be possible to proceed with the treatment, provided that one works slowly and with every precaution. If rabbit or beef serum is available, that can be tried. However, if the reactions to small preliminary doses are severe, one should recognize that to take a chance on the results of failing to administer serum may be better than to kill the victim forthwith. In desperate cases, the patient may be desensitized.[34]

The injection of epinephrine (adrenalin) solution at the same time as the injection of serum, or the addition of epinephrine to a dilution of serum with physiologic saline, is to be considered if sensitiveness is demonstrated. It has two objections: the injection of epinephrine to a nonasthmatic person may induce a severe adrenergic reaction, with shaking, palpitation, rise in blood pressure and even disturbance of the heart rhythm; and the epinephrine may postpone and mask the onset of a reaction until an overwhelming dose of serum has been administered. I believe that epinephrine should not be given until the reaction begins, but that it should then be injected at once. Epinephrine should take effect within five minutes, and the prompt injection of a small dose (0.5 cc. of a 1:1000 dilution) should suffice. To give more than 2.0 cc. of epinephrine hydrochloride subcutaneously in one hour may be dangerous.

Prevention and Treatment of Tetanus

Prevention

The prevention of tetanus at the time of injury of a person who has not been previously immunized with tetanus toxoid is accomplished best by the prompt administration of tetanus antitoxin, as stated above. However, active immunization with tetanus toxoid, will, it is hoped, be a matter of universal application in the near future. In 1923, Ramon[44] discovered that when diphtheria toxin was treated with formalin, it lost its toxic properties without losing its antigenic capacity, and Descombey[45] found this to be true for tetanus. Ramon and Zoeller[46] published several papers on the use of what they called "anatoxin" to produce active immunity to tetanus in man.

The results from active immunization against tetanus are most satisfactory. Rouques[47] has reported that by May, 1939, approximately 1,500,000 soldiers in France had been immunized with tetanus toxoid, and up to the time of his writing, no case of tetanus had been reported among them. Other and similar reports can be anticipated. When normal subjects are given two injections of alum-precipitated tetanus toxoid at intervals of two to eight weeks, — the average is about a month, — tetanus antitoxin develops in the blood. Gold[48] has shown that the alum-precipitated ma-

terial gives better results than plain toxoid, presumably because it is absorbed more slowly and over a longer period. After the first dose, the response is small, but after the second the antitoxic content increases markedly, as Jones and Moss[49] showed. In an earlier paper, Gold[50] found that this antitoxin content tends to fall again in the course of months. If, however, at the time of injury an additional dose of toxoid is administered to these pretreated persons, the antitoxin returns very promptly, and the titer becomes higher than ever. Since, according to a recent announcement,[51] all United States soldiers are to be immunized against tetanus, only those casualties whose wounds have been grossly contaminated with material suspected of containing tetanus spores will require other than an injection of tetanus toxoid.

Reactions to tetanus toxoid, particularly to the second dose, have caused some difficulty. Anaphylaxis has been reported. In 1940, Cooke and his associates[52] described a forty-four-year-old man with asthma who was given his first dose of tetanus toxoid in June without symptoms. In October, the second dose was followed in fifteen minutes by a constitutional reaction, with severe urticaria, edema of the face and prostration. Skin tests with the pure materials used in making the toxoid were applied, and large reactions were obtained to the peptone used in the broth, as well as to the toxoid itself. In 1940, Parish and Oakley[53] observed a patient who did not give any history of allergy, but who nevertheless reacted in ten minutes in the same way as Cooke's patient did; furthermore, when an intracutaneous test with Witte peptone was applied, another constitutional reaction ensued.

Reactions to tetanus toxoid, however, are not common. Whittingham[54] was able to collect only 14 cases (0.023 per cent) among 61,042 persons immunized with two doses. Hall,[3] who has had a large experience with tetanus toxoid in the United States Navy, says little about peptone as a cause of reaction, but he has observed that one lot of toxoid gave reactions (mostly sore arms) in 50 of 1800 second injections, whereas another lot of toxoid gave no reaction in any of the 743 midshipmen treated. He found that the first lot contained more total nitrogen than the second lot, and that it reacted with the protein color tests. The only difference between the two lots was in the manner in which the alum precipitate had been washed. If the reactions are due to peptone in the broth used for growing this organism, it is very strange that guinea pigs sensitized by Hall's alum-precipitated tetanus toxoid did not react to alum-precipitated diphtheria toxoid or vice versa, whereas members of each group of animals died at once in anaphylactic shock when reinjected with the original sensitizing material.

Is it always safe to give the second dose of tetanus toxoid? Should one always inject a small quantity of the material into the skin itself, to be sure that there is no reaction, before administering the whole of the second dose? This would be playing safe, of course, but since sensitiveness is so rare and reactions are so few, it is probably sufficient in actual practice to inquire about reactions to the first dose of toxoid and then to consider whether the patient has an allergic history. If there is any doubt, however, a skin test takes only a little time and is very easy to perform.

Treatment

The treatment of active tetanus is always difficult, and the mortality ranges between 30 and 90 per cent according to different authors. As Zinsser, Enders and Fothergill[1] write, "A review of mortality statistics does not impress one regarding the value of antitoxin." They point out: "The effect of antitoxin is probably limited largely to neutralization of uncombined toxin circulating in the blood stream and lymphatics. . . . For this reason, its use as a therapeutic agent is definitely indicated." They condemn the injection of antitoxin either into the spinal canal or into the cisterna, for "to reach the motor cells, the injected antitoxin would have to pass the pial membrane and be absorbed across a large space of tissue." Through the blood stream, however, the serum can reach the motor cells quickly and easily.

Quite recently, three papers described a similar and quite new conception of the treatment of tetanus. These papers were written at about the same time. No one of them refers to the others, and it is quite interesting that each of the authors arrived at about the same conclusions and quite independently. Each uses antitoxin intravenously in large doses and then gives heavy sedation. Vener and Bower[55] advocate an initial dose of 100,000 units of tetanus antitoxin intravenously, and a total dose of about 200,000 units. Of 100 patients, 12 died within the first twenty-four hours of treatment, but of the 88 who survived the first day, only 17 died—a mortality of only 20 per cent. Chapman and Miller[56] give a graphic description of a heroic and victorious struggle with the disease in a boy of ten. They emphasize six principles in treatment. The first is not antitoxin but sedation, and they used large and almost continuous doses of luminal sodium and morphine. The second is surgical removal of the focus, and the third is antitoxin, which they give intravenously in moderate doses, 20,000 to 40,000 units at intervals during the first

few days. Lumbar puncture was used frequently for restlessness and convulsions, evidently because of increased intracranial pressure. Finally, they lay great stress on general care: on oxygen for cyanosis; on aspiration of nasal mucus to clear the airways; on food and water by nasal catheter to maintain nutrition; and on constant attendance by skillful nurses. The third paper is by Spaeth,[57] who also uses 30,000 to 60,000 units as a first dose. He too emphasizes heavy sedation and lays great stress on skillful care, with expert attention to every detail of medical and surgical management. In a hospital as large as the Cook County Hospital in Chicago, he advocates special tetanus teams of highly trained nurses. As a result of the new methods of treatment, the danger of tetanus has been modified greatly. The experience in Chicago is a large one, and the conclusions of Spaeth deserve attention. Mild tetanus, without convulsions, is not fatal. Moderate tetanus with spasm but without cyanosis occurred in 32 patients, 2 of whom died. Severe tetanus is the real problem. Before the modern technic, 109 patients (95 per cent) died in a group of 114, but with the new methods only 32 (74 per cent) died out of 43. In total, the mortality from tetanus at Cook County Hospital has fallen from 67 to 35 per cent. Whoever is called on to treat a patient with active tetanus should read each of these three papers carefully.

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CASE RECORDS OF THE MASSACHUSETTS GENERAL HOSPITAL

ANTE-MORTEM AND POST-MORTEM RECORDS AS USED IN WEEKLY CLINICOPATHOLOGICAL EXERCISES

FOUNDED BY RICHARD C. CABOT

TRACY B. MALLORY, M.D., *Editor*

CASE 28181

PRESENTATION OF CASE

A fifty-three-year-old single clerical worker was admitted to the hospital because of nausea.

She had been in good health until a month before entry, when she developed nausea after eating that was occasionally followed by vomiting. The vomiting occurred as often as three times a week, and was not associated with pain, gaseous distress or other symptoms. The bowels were regular, and the appetite was good, although 10 pounds of weight had been lost in the course of the month. A week before entry, a physician prescribed liver and iron therapy; he told the patient that she had been having "glycosuria for several years."

The patient's father died at fifty-nine years "in diabetic coma."

On admission, the patient appeared well developed and nourished, with striking pallor of the skin. The mouth was edentulous. The breasts, heart and lungs were normal. The abdomen was soft, with a movable mass extending upward from a point just below the umbilicus; this seemed to join with a second mass that lay just beneath the left costal margin. The left border of the masses seemed quite discrete.

The blood pressure was 140 systolic, 90 diastolic. The temperature, pulse and respirations were normal.

Examination of the blood showed a red-cell count of 3,150,000 with 8.4 gm. hemoglobin, and a white-cell count of 12,400, with 74 per cent polymorphonuclears, 18 per cent small lymphocytes and 6 per cent monocytes. The blood Hinton reaction was negative. The hematocrit was 33 per cent. The prothrombin time was normal. The urine was normal on two examinations. The stools were guaiac negative.

Roentgenograms of the gastrointestinal tract showed a normal stomach and duodenum. One of the upper loops of jejunum showed pressure of an extrinsic mass; the upper loops were slightly dilated. The two-hour film showed most of the barium beyond a lobulated mass, 15 cm. in diameter, lying in the left midabdomen. One loop of bowel appeared involved by the mass, since this loop retained barium for five hours. The margins of the bowel were irregular and serrated, and there seemed to be swelling of the mucosa, without definite obstruction. The lower ileum and colon appeared normal, although the mass seemed to press slightly on the upper descending and transverse portions of the colon.

Two days later, additional roentgenograms were taken with a Rehfuss tube passed into the third portion of the duodenum. The first loop of jejunum again appeared dilated. The second loop ran around a mass and showed marked disturbance of its mucosal pattern. No definite folds were seen. Fine sinuses appeared to run away from the lumen. The abnormal area extended approximately 16 cm. The lower small intestine seemed normal, barium reaching the ileocecal valve in twenty minutes.

On the ninth hospital day, an operation was performed.

DIFFERENTIAL DIAGNOSIS

DR. ROBERT R. LINTON: I must admit that I have not a great deal to go on in this patient except that she had nausea and vomiting of a month's duration. She was fifty-three years of age and came in with a tumor in the left upper quadrant. The description on physical examination is different from that on x-ray examination, and I think one must realize that in the latter the mass chiefly noted was probably the lower one.

Let us approach this by considering tumors of the left upper quadrant. The first one that enters my mind, since the upper mass was at the left costal margin, is the spleen. I cannot connect the spleen with a mass separate from it and extending below the umbilicus. We have no history of malaria or any other disease that might incriminate the spleen, and I think that the spleen can be ruled out. It is possible that the patient had an aneurysm of the abdominal aorta, but such an aneurysm would not be freely movable and would be a pulsating mass. Therefore, I can rule out aneurysm. It might be a kidney tumor, because kidney tumors can present anteriorly as well as posteriorly, but again we have nothing to incriminate the kidney. The urine examination was negative. No intravenous pyelograms were done, or reported at least; and I therefore think that a kidney lesion can also be ruled out. One must consider a number of conditions in the gastrointestinal tract, but before going on to those I might ask Dr. Holmes to show us the x-ray films. Do you know whether the barium reached the ileocecal valve in twenty minutes after it was taken by mouth?

DR. GEORGE W. HOLMES: I do not believe so. I think the last statement refers to an enema for

the small bowel, which Dr. Schatzki has recently been working on.

We have fairly good evidence that this patient had a lesion involving the small bowel and primary either in the small bowel or in the abdomen outside the small bowel. The stomach and colon were normal. There is nothing abnormal about the appearance of the liver and spleen, according to the x-ray films. The kidneys are not well visualized. There is no evidence of any disease of the bone. In this first film, one sees dilated loops of small bowel, which are definitely abnormal, and in this one, taken when the barium was leaving the stomach, the loops are rather large and the barium has a tendency to pile up in that area. A little later, one sees retention of barium, and a rather ragged indefinite margin in the same position. In twenty-four hours, there are some traces of barium in the small bowel. From this examination alone, we have very good evidence of a small-bowel lesion. This next group of films, taken after the injection of the barium through the tube, shows a definitely deformed loop of small bowel. Lesions of the small bowel often show quite extensive involvement of the mucosa but do not of necessity produce obstruction. This one did, and there is no question about the involvement of the mucosa. As I read the note, I got the impression that there was some evidence of another lesion in the small bowel, but I cannot find it offhand. The lower small bowel seems to be normal. In other words, I do not believe this is the so-called "ileitis." It does not look like that. It is some form of tumor. It could be tumor outside involving the bowel, or it could be a tumor involving the bowel from the inside.

Dr. William B. Breed: Can you demonstrate the displacement by the mass that was palpated? I do not see that.

Dr. Holmes: I do not see it either. I think one would have to fluoroscope the patient to be able to visualize it. In these films, it is not obvious.

Dr. Linton: Another condition I had considered is pancreatic cyst, but I believe the fact that the jejunum beyond the ligament of Treitz for a considerable distance is involved rules out the question of pancreatic cyst. Also, the fact that it was movable eliminates such a cyst, because the pancreas is a rather fixed retroperitoneal structure. The conditions one must consider are: carcinoma, lymphoma, congenital abnormality and infection.

Carcinoma of the jejunum is a fairly rare disease, but it does occur. Carcinoma of the jejunum, however, would produce a localized lesion, with complete obstruction rather than a lesion that extended over perhaps 16 cm. of the bowel with only partial obstruction. The other thing that seems strange, if it should prove to be carcinoma, is that the stools were guaiac negative. Certainly, with an ulcerated lesion, one would expect at least microscopic blood in the stools.

Was this a lymphoma of the small bowel? I am unable to rule it out, and I think that this diagnosis should be seriously considered. The patient had a low red-cell count and hemoglobin and not a very significant white-cell count.

One other condition that I should consider much more seriously if this were a child rather than an adult is so-called "enteric cyst" or reduplication of the intestinal tract. It seems unlikely that the patient would live fifty-three years without getting into trouble from such a cyst, and I think one would have to exclude it on that basis. Then there is the mesenteric cyst, which is different from an enteric cyst or reduplication of the intestinal tract since it is localized in the mesentery instead of involving the bowel wall. That seems to me to be a possibility. The only thing that seems doubtful about that diagnosis is the fact that in the last x-ray film fine sinuses appeared to run outward from the lumen of the bowel; this suggests to me that there was destruction of the bowel wall or intestinal mucosa, with sinuses running away from it. I remember a case similar to this in a patient who ate a piece of porcupine quill, which stuck in the upper jejunum and produced an abscess. One can rule out the question of foreign body with abscess because the patient had a freely movable mass, no fever and no leukocytosis.

In conclusion, I believe that this was a lesion of the bowel, involving the bowel wall and the bowel lumen, with partial intestinal obstruction. The only way to be absolutely sure what the condition is is to open the abdomen. I hazard the guess that this patient was suffering from lymphoma of the small bowel.

A Physician: Would not the appearance of the serrated small bowel be against anything like cyst?

Dr. Linton: I should think so, except an enteric cyst, and the patient is too old for that.

Dr. Tracy B. Mallory: The X-ray Department expressed a preference for regional enteritis. Do you want to comment any further about that, Dr. Holmes?

Dr. Holmes: I think they had a decided advantage over me, and I hesitate to disagree with them. Of course, with a multiple lesion, enteritis should always be seriously considered.

Dr. Linton: I intended to discuss regional enteritis. It seemed a definite possibility in view of the x-ray picture. The thing against it is the short duration of the history and the localization of the

lesion in the jejunum, although I am aware that it may occur in this location.

DR. CHESTER M. JONES: It tends toward fistula formation.

DR. ALLEN G. BRAILEY: I think we should re-emphasize the points that Dr. Jones and Dr. Richardson made two weeks ago when I discussed a case — namely, guaiac-negative stools do not rule out ulcerative lesions in the mucosa, and furthermore the rather extreme anemia means that the patient had been bleeding, probably for some time.

CLINICAL DIAGNOSIS

Lymphoma of jejunum?

DR. LINTON'S DIAGNOSIS

Lymphoma of jejunum.

ANATOMICAL DIAGNOSIS

Carcinoma of jejunum.

PATHOLOGICAL DISCUSSION

DR. MALLORY: Dr. Richard H. Sweet, who operated on this patient, is not here. Can you describe the findings at operation, Dr. Brailey?

DR. BRAILEY: The upper 46 cm. of the jejunum was moderately dilated and injected and quite definitely edematous. Then, about 16 to 18 cm. of jejunum was of normal contour but of smaller size, firm, deep red and speckled with implants. The lymph nodes of the mesentery were involved. The second mass described was a large carcinomatous implant in the mesentery.

DR. MALLORY: The preoperative diagnosis was the same as Dr. Linton's, — lymphoma of the small bowel, — but at operation it was obvious at a glance that it was cancer, primary in the jejunum; that diagnosis was proved by biopsy. It was quite beyond the realm of resection, and a side-to-side anastomosis was done to relieve obstruction.

CASE 28182

PRESENTATION OF CASE

A sixty-year-old housewife consulted a physician because of numbness in the right leg for a week, and because of various "heart symptoms" of much longer duration.

At least twenty years previously, the patient had been told that she had "heart disease," and on one occasion had been refused life insurance because of it. She frequently visited a health resort. On her last trip to that institution, seven months previously, she had been told that she had auricular fibrillation, with a systolic blood pressure ranging up to 165. At that time, she complained of shortness of breath on exertion, palpitation and precordial soreness. These symptoms persisted. About six months later, the patient noted for the first time an ache in the upper part of the left arm. This remained constant, becoming worse on exertion. After four weeks, there was a very severe exacerbation of this pain. At about the same time, a cold feeling became manifest in the right leg. This was followed by a persistent numbness in the leg, but no actual pain. During this period, the patient took digitalis.

At the age of twelve years, the patient had "growing pains," but she never was aware of frank rheumatic fever. The family history was of interest, in that the patient's mother died following an amputation for an embolus.

On examination, the patient appeared rather pale, with marked engorgement of the neck veins. The heart was enlarged to the left, with the border of dullness 8.5 cm. from the midsternal line in the fifth interspace. A systolic murmur was heard in the aortic area, without associated thrill transmission to the neck. There was a slight systolic murmur at the apex, with a definite presystolic rumble. The pulse was grossly irregular, at 76. The blood pressure was 135 systolic, 70 diastolic, in each arm, although the pulse seemed stronger in the right arm than in the left. The lungs were essentially normal, as was the abdomen. There was slight pitting edema of the shins. The right leg was noticeably colder than the left. Pulsations of the dorsalis pedis artery were palpable in the left foot, but not in the right. Blood-pressure oscillations were present in both legs, less noticeably on the right than on the left.

An electrocardiogram showed auricular fibrillation, with a rate of 70. The T waves were diphasic in Lead 1, with sagging ST segment, but there was marked and deep inversion of the T waves in Leads 2 and 3. In Lead 4, the R wave was present, and the T wave was diphasic. This record was similar to one taken seven months earlier, except for deepening of the T waves, both in Lead 2 and in Lead 3.

The patient was maintained on digitalis and at rest. After two weeks, she experienced sudden onset of sharp pain over the left chest anteriorly. The respirations became shallow, and were accompanied by pain at the left costal margin and in the precordium, which was relieved by a binder. She then began to have pain in the left leg.

On examination two weeks after the onset of this last set of symptoms (a month after she was first seen), the patient was fibrillating with a rate of 70. The same murmurs were heard as previously described. There was marked bronchial breath-

ing over the left lower-lung field, with dullness. There was slight tenderness in the right calf and over both saphenous veins.

The temperature was normal, and the respirations were somewhat elevated. The blood pressure was 145 systolic, 90 diastolic.

Two days later, the patient complained of pain in the abdomen, without apparent localization. Extreme dyspnea appeared quite suddenly. The patient appeared pale, with cyanosis of the lips and fingertips. Death occurred several days later.

Differential Diagnosis

Dr. Robert E. Glendy: We can draw some immediate conclusions from this case history, I believe: the patient had rheumatic heart disease of long standing, with cardiac hypertrophy, mitral-valve and possibly aortic-valve involvement, auricular fibrillation and, for some time, considerable impairment of myocardial reserve, manifested by dyspnea on effort and later by peripheral edema, which may have been the result of peripheral vascular disease; however, toward the end of her life, she had multiple embolic manifestations, presumably from both sides of the circulation.

Although the precordial soreness, pain in the left arm and the bait thrown out in the report of the electrocardiogram tempt one to consider myocardial infarction with mural thrombus formation as a possible source of emboli, the clinical manifestations were too vague, and it is likely that the T-wave changes in the electrocardiogram were due to digitalis instead of myocardial infarction. The patient was well into the coronary age group, but I am willing to discard coronary disease as an important factor. However, an infarct involving the septum of the heart with mural thrombi on either side could conceivably account for embolic manifestations on both sides of the circulation.

It appears that until four or five weeks before the patient consulted her physician, the symptoms were those of a gradually diminishing cardiac reserve. Then she developed an aching pain in the left upper arm, constantly present, but worse on effort — presumably, effort involving the arm — and lasting four weeks, at the end of which time there was a severe exacerbation of the pain. There is no further mention of this pain, and the only clue we have regarding it is the statement that "the pulse seemed stronger in the right arm than in the left." In view of subsequent events, it is fair to assume that the symptom was due to an embolus to the left arm that impaired the circulation sufficiently to cause pain but did not endanger the nourishment of the tissues because of the free anastomotic circulation in the arm. The exacerbation of the pain was probably due to propagation of a thrombus proximal to the embolism; such propagation often occurs. Next, the patient developed numbness and coldness in the right leg, the latter being confirmed on physical examination, and pulsations of the dorsalis pedis artery could not be felt in the right foot. Here again, the circulation to an extremity was impaired, I believe, by an embolus, but not sufficiently to necessitate or warrant any drastic measures to save the affected part. These two emboli found their way into the peripheral circulation by way of the left side of the heart, and of necessity came from either the pulmonary veins or the chambers of the heart itself. Assuming that the septal tissues were intact, the most likely source was from an auricular thrombus.

After about two weeks, the patient developed a sudden sharp pain over the left chest, with respiratory embarrassment, and in the course of time was found to have signs of consolidation in the left lower lung. I should interpret this episode as one of pulmonary infarction from an embolus. With pain in the left leg and tenderness in the right calf and over both saphenous veins, thrombophlebitis in the deep and superficial veins of the lower extremities seems a likely source of such an embolus. In the presence of any sort of septal defect, venous thrombosis in the extremities might, in fact, account for all the embolic manifestations in this patient, but I do not believe such a defect was present here.

The terminal symptoms included unlocalized abdominal pain, sudden extreme dyspnea, pallor and cyanosis. The abdominal pain may very well have been the result of the migration or propagation of a large thrombus from either extremity or from the pelvic veins. The sudden dyspnea and circulatory collapse, from which the patient died, I should interpret as due to massive pulmonary infarction from an embolus arising in the deep venous circulation.

If I am correct in my analysis of this case, postmortem examination should reveal: rheumatic heart disease, myocardial hypertrophy, mitral stenosis and regurgitation, possibly slight aortic stenosis, evidence of mural thrombi in the left auricle, thrombophlebitis of the deep and possibly the superficial veins of the lower extremities, — with a free or propagating thrombus in the larger venous radicles, — multiple pulmonary infarcts and evidence of peripheral embolism to the right leg and left arm.

Dr. Paul D. White: I should like to ask Dr. Glendy if he thinks the engorgement of the neck veins noted on first examination and the changes in T waves might be due to a dilatation of the right ventricle, not wholly from failure but perhaps

from a previous episode of pulmonary embolism.

DR. GLENDY: I think that is true. All we have to go on so far as previous pulmonary infarction is concerned is the condition of the lungs reported on the first examination and said to be essentially normal. Of course, I suppose it is possible to have pulmonary infarction of sufficient degree to produce such a picture, but it does not seem likely in view of the fact that the lungs were reported normal.

DR. WHITE: It would help to explain the electrocardiogram.

DR. GLENDY: Yes.

CLINICAL DIAGNOSES

Rheumatic heart disease.
Mitral stenosis and insufficiency.
Slight aortic stenosis.
Auricular fibrillation.
Coronary insufficiency?
Embolus, right leg.
Phlebitis.
Pulmonary infarct.

DR. GLENDY'S DIAGNOSES

Rheumatic heart disease.
Myocardial hypertrophy.
Mitral stenosis and regurgitation.
Slight aortic stenosis?
Mural thrombi, left auricle.
Thrombophlebitis, lower extremities.
Multiple pulmonary infarcts.
Embolism, right leg and left arm.

ANATOMICAL DIAGNOSES

Coronary thrombosis.
Infarction of heart, old and recent.
Endocarditis, chronic, rheumatic, with mitral stenosis (severe) and aortic stenosis (slight).
Pulmonary embolism.
Pulmonary infarction.
Pleural effusion, left.
Thrombosis, popliteal veins, bilateral.
Embolism, popliteal artery, right.
Infarct of kidney, right.

PATHOLOGICAL DISCUSSION

DR. TRACY B. MALLORY: Post-mortem examination bore out most of Dr. Glendy's predictions. It showed a little more as well. There was an old rheumatic heart disease, with a fairly severe mitral stenosis and also involvement of the aortic valve, although not enough, I should think, to be functionally significant. There was also severe coronary sclerosis, with diffuse atherosclerotic narrowing of all the branches and a fairly recent thrombosis in the right coronary artery. Consequent to this was a focus of infarction in the posterior wall of the left ventricle, with an overlying thrombus. There was no thrombus in the auricle. The embolus was found in the right popliteal artery. Unfortunately, the left brachial artery was not examined, so that we cannot say whether there was or was not an embolus. Almost certainly, the source of the emboli was the thrombus overlying the cardiac infarct.

DR. WHITE: The thrombus in the coronary artery could not have been embolus?

DR. MALLORY: I do not believe so. It overlay an atheromatous plaque, and looked like a perfectly good thrombus of fairly recent origin. There was a small infarct in the kidney as another manifestation of embolism. Thrombophlebitis was found in the deep veins of the calf on both sides, more marked on the left than on the right. Pulmonary emboli were present. One of these had evidently occurred many days, perhaps a couple of weeks, before death and had produced a rather large single infarct of the left lower lobe. This embolus was rather firmly adherent in the branch of the pulmonary artery, and the infarct showed early signs of organization at the periphery. There had also been a shower of smaller emboli to other pulmonary vessels, particularly in the right lung, none very large, and all out in the periphery; all of them were very recent, none caused infarction, and none were adherent. That, I imagine, represents the terminal episode.

DR. WHITE: The earlier infarct might have been there prior to two weeks.

DR. MALLORY: About two weeks would be my guess on that.

DR. WHITE: After the patient was examined the first time?

DR. MALLORY: Yes; there was an episode of pleural pain at about the right time.

DR. GLENDY: What about the explanation of the phlebitis? Was there any propagation in the pelvis?

DR. MALLORY: We found nothing above the popliteal veins. One thing of a little interest was a left hydrothorax of 3500 cc.—a very large amount of pleural fluid. Usually, when unilateral hydrothorax is present, it is on the right, but in this case the right pleural cavity was dry. Small pleural effusions do occur secondary to infarction, but we have never seen a pleural effusion approaching the size of this one that we should heretofore have attributed to infarction.

DR. WHITE: Did you state the age of the myocardial infarct?

DR. MALLORY: The sections show both old scarring and fairly fresh necrosis. I cannot estimate its age with any accuracy.

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PROCUREMENT AND ASSIGNMENT SERVICE

The enrollment forms and the questionnaires for the Procurement and Assignment Service have been or are about to be forwarded to every registered physician in the United States. The need for medical officers in the armed services is acute, and at the same time medical services to other governmental agencies, industry and civilian communities must be provided or maintained. Hence, all physicians, regardless of age, sex, race, physical condition, citizenship or employment, and regardless of any enrollment forms or questionnaires that have previously been made out, should carefully fill out these forms and IMMEDIATELY return them in the envelopes that are enclosed, which require no postage. Only with the information that will be obtained from these forms by the National Roster of Scientific and Specialized Personnel, which will be made available to the Procurement and Assignment Service, can the latter intelligently and expeditely perform its functions, which are so vital to the war effort.

"HOLD FAST THAT WHICH IS GOOD"

A Europe in ruins laments the wanton destruction of the physical monuments of its civilization. Cathedrals are reduced to rubble; art galleries are destroyed, and their treasures of painting and sculpture burned, broken or ravished; schools, hospitals, reservoirs, railways, all the implements of civilization are scattered upon the blasted earth, whose peoples succor their wounded and lament their dead. And all because a paranoiac person with a messianic megalomania has indoctrinated a part of a great nation with a passion for the satisfaction, by ruthless force, of spurious grievances, and has cowed the rest into subservient support of his infamous ambitions.

Libraries have not escaped this holocaust. Louvain, barely rebuilt since the *furor Teutonicus* razed it, has again been leveled. The Royal College of Surgeons is in ruins — its priceless literary treasures, its collections prepared by the very hands of John Hunter, its medical memorabilia blown to bits. The University of Paris has been robbed for the enrichment of the seats of spurious learning of the self-styled Nordic superman, whose servile sycophantic scholars pervert and falsify the accepted facts of history and science to give plausibility to his monstrous ideology.

We in America, so remote geographically from the lair of this Caliban of civilization on the East and from his infamous imitators to the West, cannot believe that our homes and treasure houses are in real danger of physical destruction. Perhaps we are right; or perhaps we have learned nothing from Pearl Harbor and Bataan. Be that as it may, there are other dangers, insidious but fatal. A library may be demolished by a bomb, or it may suffer slow and deadly decay from neglect. We are bringing all our resources — mental, physical and

financial — to the winning of a free way of life for the peoples of the earth. It would be folly to lose through indifference the fruits of years of patient effort. Such fruits are perishable; they cannot be left unwatered for the duration of the national emergency with the expectation that they will be found sound and nourishing afterward.

Such an institution is the Boston Medical Library, whose present situation and prospects are described in the annual report of its president elsewhere in this issue of the *Journal*. It deserves and should receive, in some form or other, the support of every reputable physician in Boston — or, rather, in New England. Those who are fellows should not withdraw unless forced to by dire necessity; those who are not should seek fellowship. All should encourage it by entering its house to enjoy its privileges and by spreading abroad its good report. The purpose of its custodians has not changed since Dr. Chadwick, some sixty-four years ago, in the third year of its existence, wrote the first request for funds: "With this record of past achievements, the Association now appeals for aid to meet its present wants, and to provide for its immediate entrance into a wider sphere of prosperity and usefulness."

TYPHOID CARRIERS

THE day is past when typhoid fever is being spread in large epidemics by water and milk. Safeguards now thrown around such supplies eliminate the possibility of large epidemics, and small ones are becoming exceedingly rare. Although, since 1915, the disease has decreased in Massachusetts from the level of over 2000 cases a year to less than 100 a year, there is no expectation that it can be completely eliminated, because numerous sources of infection are still present.

It is a well-established fact that more than 3 per cent of the persons who contract typhoid fever continue to harbor typhoid bacilli during the remainder of their lives, usually in the gallbladder but sometimes in other foci. In the years when the prevalence of typhoid fever was high, facilities to detect convalescent carriers by proper laboratory supervision of recovered cases were not available. Consequently, many of those who had the disease in the past now harbor virulent typhoid bacilli in their intestinal tracts and many of the typhoid cases of the present day are due to contacts with such persons. From time to time, estimates have been hazarded regarding the number of typhoid carriers now present in Massachusetts. These estimates have varied within considerable limits, but there are probably at least 1500 such carriers in the State today. Only one tenth of these cases are on the records of the Department of Public Health, and most of these were discovered in the investigation of reported cases.

It is therefore not surprising that occasional incidents such as those described in a paper in this issue of the *Journal* occur from time to time. Most physicians are familiar with the fact that the typhoid bacillus is one of the etiologic agents of cholecystitis. Nevertheless, when a disease is at as low a prevalence as typhoid fever is today, this fact is easily forgotten. In such cases, failure to observe strict precautions may result in the infection of a nurse or a house officer.

From the much publicized story of Typhoid Mary,[1] it is the usual impression that typhoid carriers are very dangerous, causing numerous cases of the disease. Fortunately, in an area where public sanitation and personal hygiene are at as high a level as in New England, it is unusual for such persons to cause cases. Some have gone as long as thirty and forty years without apparently having ever given rise to a single case. The fact that 1500 carriers in Massachusetts are producing only about 75 cases of typhoid fever a year bears out this statement.

So long as typhoid fever continues at its present low rate of prevalence, current cases will produce only a few carriers each year. Furthermore, most of the carriers in the State are persons who had their typhoid fever many years ago and are, consequently, dying off at a high rate. It is therefore to be expected that the disease will drop to even lower levels than those prevailing at present, in

spite of the migration of occasional carriers into the State from areas of higher prevalence.

Physicians treating cases of cholecystitis should make careful inquiry concerning previous typhoid fever. When a past history is elicited, careful laboratory studies should be made to exclude the carrier state. Such preventive measures will disclose additional carriers and eliminate the chance of infecting contacts in the home and in the hospital.

Recently, the investigation of a case of typhoid fever in a child disclosed the grandmother as the source of infection.[2] The child became ill a few months after the grandmother had been in a hospital where she was under treatment for cholecystitis and cholelithiasis. A careful history at the time of this admission would have disclosed an attack of typhoid fever many years before. Laboratory study would have revealed the carrier condition and prevented a possible death from typhoid fever.

REFERENCES

1. Soper, G. A. The curious career of Typhoid Mary. *Bull. New York Acad. Med.* 15:698-712, 1939.
2. Massachusetts Department of Public Health. Unpublished data.

MEDICAL EPONYM

OPPLER-BOAS BACILLI

These were described by Bruno Oppler, a Berlin gastroenterologist who had been an assistant of Ismar Boas (1858) in the Polyclinic, in the *Deutsche medicinische Wochenschrift* (21:73-75, 1895). The title of the article containing the description is "Zur Kenntniss des Mageninhalts beim Carcinoma ventriculi [On the Recognition of Stomach Contents in Carcinoma Ventriculi]." A portion of the translation follows:

> Uncommon as it is to find an entire absence of microorganisms in the microscopic examination of the stomach contents, it is even rarer that they dominate the field of vision at the expense of all other elements. Leaving yeast and sarcinas for the present out of consideration, up to the present time I have practically found this only in carcinoma. Here there is an apparently quite definite variety of rather slender bacilli, which are grouped in long threads and zigzag lines that so dominate the field that they fill the spaces between the other elements (food particles and so forth) and at times are matted together in thick bundles. Presumably, this is a saprophyte. . . . This luxuriant bacterial growth is particularly seen in carcinomas when the stomach contents show, together with the absence of free hydrochloric acid, the signs of very much diminished motility: that is, in those cases in which lactic acid is produced. I have sought for them in vain in the stagnant stomach contents of benign pyloric stenosis or atonic gastrectasis, although, to be sure, these usually contain abundant free hydrochloric acid.

R. W. B.

MASSACHUSETTS MEDICAL SOCIETY

COMMITTEE ON MATERNAL WELFARE

CASE HISTORY: TOXEMIC PREGNANCY FOLLOWED BY UNSUCCESSFUL OPERATIVE DELIVERY AND DEATH

A thirty-four-year-old primipara was sent into the hospital a week before expected labor because of a blood pressure of 130 systolic, 80 diastolic, and a large trace of albumin. She had not been seen during her pregnancy until this date. The past history was essentially irrelevant. The heart and lungs were normal, the uterus was enlarged to a size compatible with term, and the fetal heart was audible. On admission the patient was put to bed and treated medically for this mild toxemia. The blood pressure is said not to have risen any higher, although albuminuria was constant. There was a good deal of swelling in both legs. Six days after entry, labor started spontaneously, and at the end of twelve hours the cervix is said to have been fully dilated. Because of lack of progress, a forceps delivery was attempted but was unsuccessful. Another operator attempted version, which was likewise unsuccessful. By this time, the patient's general condition was poor, and the pulse was rapid, although there is no mention of external bleeding. A consultant was called eight or ten hours later, but the patient died undelivered before his arrival.

Comment. This whole case represents atrocious obstetrics. Only the hospitalization and rest in bed for a week before the onset of spontaneous labor are to be commended. It is perfectly possible that the pelvis was not adequate for this particular baby, or that the attempt at forceps delivery failed solely because of the lack of skill on the part of the operator. Had the patient been intelligently observed after the forceps delivery had proved unsuccessful, it would not have been too late to perform an extraperitoneal cesarean section. The unsuccessful attempt at version emphasizes the inadequacy of the medical care. It is possible that in the attempt at version the uterus was ruptured and that death, which occurred several hours after this operation, was due to continued bleeding into the peritoneal cavity.

Such obstetric mismanagement would not occur in any hospital where adequate supervision is routine, and the death was, of course, avoidable.

WAR ACTIVITIES

CIVILIAN DEFENSE

Plan to Establish Blood Banks

Hospitals in communities exposed to war hazards may receive assistance in the establishment of a blood and plasma bank through funds available to the United States Public Health Service, which will be administered by it through the Medical Division of the United States Office of Civilian Defense. In addition to providing whole blood or liquid plasma for the current needs of hospitals, these blood banks, as well as others already in operation, are to accumulate a reserve supply of plasma for civilian casualties caused by enemy action. Technical and bacteriologic safeguards are to be observed, as recommended by the Subcommittee on Blood Substitutes, Division of Medical Sciences, National Research Council. At the request of the Office of Civilian Defense, a technical handbook on blood and plasma banks has been prepared by this committee, which will be distributed by the Office of Civilian Defense to hospitals.

Following the advice of the committee of the National Research Council, financial and technical assistance will be provided to only three hundred hospitals of 200 or more beds approved by the American College of Surgeons and the Hospital Register of the American Medical Association. These hospitals will agree to maintain required technical standards and to accumulate a surplus of liquid or frozen plasma amounting to one unit per bed within three months. Grants will be made only for the purchase of essential equipment if obtainable locally and for sufficient technical assistance to initiate the project. Hospitals will thereafter be expected to continue to maintain the blood and plasma bank to meet their daily needs as well as the plasma reserve for civilian casualties.

Technical guidance has also been made available through the appointment of Dr. John B. Alsever, of Syracuse, New York, by Surgeon General Parran, of the United States Public Health Service, and his assignment to the Medical Division of the Office of Civilian Defense as technical director of its blood and plasma service. Dr. Alsever will be assisted by regional technical consultants in various parts of the country, whose consulting services will be made available to hospitals in their area.

As a further safeguard for the civilian population, the United States Public Health Service is providing for the production of 50,000 units of dried plasma or human albumin in laboratories approved for the manufacture of biological products by the National Institute of Health. The American Red Cross has agreed to collect the blood for this purpose without interference with its blood-collecting services for the armed forces. This second reserve of dried plasma will be distributed to Office of Civilian Defense depots located in various parts of the country. It will be made available by the Medical Division of the Office of Civilian Defense to stricken communities for their casualties whenever their own local stores of liquid or frozen plasma are in danger of being depleted.

Regional medical officers of the Office of Civilian Defense, who are appointed in the Public Health Service, will be the regional representatives of both agencies for this program. State chiefs of Emergency Medical Service or their deputies may also be appointed consultants or commissioned in the Public Health Service, so that they may act as state representatives for the two agencies in the organization of emergency hospital facilities and the reimbursement of hospitals for the care of civilian casualties. In the more populous coastal states, a full-time state hospital officer may be needed, who will also be eligible for appointment in the Public Health Service.

MISCELLANY

NOTES

The sixty-seventh annual reunion and banquet of the alumni of Boston University School of Medicine was held on Thursday, April 23, at the University Club, Boston. Dean Bennett F. A. Avery stated that seventeen members of the staff of the medical school are on active duty with the armed forces and that another is doing research work at the request of the War Department. Dr. Henry M. Pollock, superintendent of the Massachusetts Memorial Hospitals, spoke on the completion of the new Evans Memorial Medical and Research Building, to be opened on May 12. The following officers were elected: Dr. John M. Wilcox, '18, of Woburn, president; Dr. Clifton B. Leech, '19, of Providence, Rhode Island, first vice-president; Dr. Eleanor B. Ferguson, '20, of Boston, second vice-president; Dr. Frank E. Barton, '24, of Boston, secretary; Dr. Kenneth Christophe, '38, of Needham, treasurer; and Dr. Milo C. Greene, '16, of Lynn and Dr. James E. Vance, '23, of Natick, directors for two years.

Boston University School of Medicine has recently received an outright gift of $10,000 from the W. K. Kellogg Foundation, Battle Creek, Michigan, to be used for student scholarships and loans, with the purpose of assisting in the training of men for military service. The money will be available on July 1, the beginning of the next fiscal year.

CORRESPONDENCE

PHYSICIANS FOR THE VETERANS ADMINISTRATION

To the Editor: The source of supply of qualified physicians for service with the Veterans Administration has, during the past several months, sustained serious inroads by the needs of the armed forces.

The Procurement and Assignment Service, established by the President, has released to all physicians in the United States a questionnaire to determine the availability of physicians for service with the Government, either in the armed forces or in the civil services. In filling out these questionnaires, physicians may designate their preference for assignment during the present war.

Physicians enter the Medical and Hospital Service of the Veterans Administration in the grade of associate physician, at approximately the same pay as a first lieutenant in the Medical Corps of the United States Army. The volume and variety of the medical activities of the Veterans Administration are approached by few if any other organizations. Abundant clinical material is afforded in all fields of medicine and surgery, except obstetrics and pediatrics. Furthermore, there is ample opportunity for research for those who are interested.

Physicians interested in receiving an appointment should write to the United States Civil Service Commission or to Major Sam F. Seeley, Procurement and Assignment Service, 601 Pennsylvania Avenue, N.W., Washington, D. C., and should also express their preference when completing the questionnaire.

Winthrop Adams, M.D., *Manager*
Veterans Administration
Bedford, Massachusetts

TYPHOID FEVER IN HOSPITAL PERSONNEL

To the Editor: Because of the occurrence of typhoid fever in hospital personnel, the attached letter was sent to the superintendents of all hospitals and related institutions

in Massachusetts. I suggest that the letter be printed in the columns of the *Journal* for the information of the physicians of the State.

PAUL J. JAKMAUH, M.D.
Commissioner of Public Health

State House
Boston

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To HOSPITAL SUPERINTENDENTS:

Cholecystitis may be of typhoid origin. Hospital personnel in charge of gall-bladder cases on both medical and surgical wards should constantly keep this point in mind. Recently, a physician in one Boston hospital and a nurse in another contracted typhoid fever because this fact was not taken into consideration.* The first case was that of a surgical house officer who developed the disease as a result of direct contact with a previously unrecognized typhoid carrier who had just undergone cholecystectomy. The second case was a student nurse who contracted the disease while taking care of a missed case of typhoid fever admitted to the surgical ward as a case of acute cholecystitis.

Exposures to such unrecognized cases of cholecystitis of typhoid origin constitute a real risk to hospital personnel. To avoid such infections it has been recommended that all cases of chronic cholecystitis with a past history of typhoid fever be placed on typhoid precautions until laboratory studies exclude the carrier state. In addition, extreme care should be exercised by those handling dressings and discharges of all other gall-bladder cases.

On several occasions in the past, this department has called to the attention of hospital superintendents the occurrence of secondary infection among persons caring for typhoid-fever cases before the disease had been definitely diagnosed. It is, therefore, evident that many hospital employees have not been sufficiently protected against typhoid fever by vaccination. Physicians, nurses, laboratory workers and ward attendants are among those requiring antityphoid inoculations.

In addition to the primary series of three subcutaneous inoculations, a single stimulating dose should be administered once a year in order to maintain a sufficiently high level of immunity. This stimulating dose may consist of either 0.5 cc. of the vaccine subcutaneously or 0.1 cc. intradermally.

In the light of present world conditions, it is to be expected that increasingly great responsibilities may come to fall on professional personnel of hospitals. It is important that every possible safeguard be provided for such workers. The proper management of persons with gall-bladder disease and those ill with fever of undetermined origin, together with antityphoid inoculation of personnel, will reduce considerably the risk of typhoid fever.

PAUL J. JAKMAUH, M.D.
Commissioner of Public Health

NOTE: Cholecystitis of typhoid origin (typhoid carrier) is a reportable disease.

*These two cases are reported and commented on editorially in this issue of the *Journal*. — ED.

REPORT OF MEETING

BOSTON ORTHOPEDIC CLUB

A regular meeting of the Boston Orthopedic Club was held at the Boston Medical Library on December 15, with Dr. Otto J. Hermann presiding. The speaker of the evening was Dr. John Scudder, of New York City, who discussed "Shock."

Studies on the ionic changes during this condition, particularly in regard to potassium, originated in the work of the botanist, Osterhout, and have been carried on by Dr. Scudder after the manner of Dr. James L. Gamble. Allusion was made to the increased-action current by an elevation of the potassium content of a system and its return to normal when sodium is introduced. The close analogy of sea water, plasma and interstitial fluid brought out by Dr. Gamble was contrasted to the great difference in cellular fluid. The deleterious effect of the potassium ion on the electrocardiogram of the cat and the saving effect of sodium or adrenocortical extract were pointed out.

Several varieties of experimental shock were shown to have the common factor of a change in the potassium ion content. Noxious stimuli are known to increase shock, which is a principle behind the deflation of intestinal obstruction. Distention of a balloon in the intestinal tract of a cat not only increases the specific gravity of the blood but also causes an elevation of the potassium content. These values return to normal only if the distention is relieved in less than thirty-six hours, but not if the condition persists over forty-eight hours. This, of course, is an important consideration in the treatment of shock. Esophageal obstruction is as fatal in the cat as that at the duodenum, with an elevation of the specific gravity of the blood thirty-six hours before any ionic changes occur. Similar electrolyte changes occur in acute pancreatitis and hemorrhage, but are measurable only late in the syndrome. The protein values change but little. The terminal outpouring of the potassium ion from the tissues occurs after all other materials have been exhausted. In experimental shock produced by trauma, there is an elevation of serum potassium that is relieved by the administration of sodium. Therefore, one variable of all types of shock appears to be an alteration of all the body fluids as well as plasma, such as the cerebrospinal, pericardial, peritoneal, lymph and tissue fluids.

Cases of shock of various sorts in human beings were cited. In a case of ruptured kidney, an early and rapid rise of serum potassium only gradually assumed normal levels. Early operations in such cases are contraindicated, therefore, and should be postponed until normal kidney function has been restored. In a case of an untreated burn, there was absorption of material from cellular breakdown causing an elevation of the potassium ion, with gradual resumption of normal levels in this strong patient. But such a recovery might not occur in all untreated patients. On the basis of these findings, dehydration therapy for severe head injuries is considered injudicious.

Dr. Scudder emphasized the significance of the electrolyte changes in shock, but pointed out that evidences of hemoconcentration are so far the earliest measurable signs of incipient or early shock. A comparison of venous and capillary blood affords a simple rough method for evaluating this factor, and Dr. Walter B. Cannon showed during World War I that values of 8,000,000 and 5,000,000 red blood cells per cubic millimeter in the capillary and the venous blood, respectively, indicate that irreversible changes have already occurred and that death is inescapable. In determining the degree of hemoconcentration as an indication of shock, Dr. Scudder suggests the use of four determinations: the hematocrit, the specific gravity of whole blood, the specific gravity of plasma and the plasma protein. Any of these alone may be misleading. Anemia may offset dehydration in the hematocrit reading, for example.

The type of therapy should be based on these findings. If hemoconcentration results in an elevation of plasma protein, it is permissible to use parenteral saline infusions prior to transfusion. On the whole, blood is the best therapeutic agent in the treatment of most cases of shock. If blood banks are used, it is essential to withdraw the blood under carbon dioxide to keep the ionic elements in their proper proportions. The use of adrenocortical extracts, as suggested first in World War I, fell into disuse for several years, but has recently been shown in histologic and clinical studies to be of definite benefit in many cases of shock. It has therefore become a useful adjunct to the armamentarium of shock therapy.

As a result of studies on electrophoretic patterns of various blood substitutes, it has been concluded that cellophane bags are not adequate for the storage of plasma. Likewise, frozen plasma has been found more stable than the liquid form. Cohn's albumin is very pure and shows definite possibilities as a blood substitute, but certain caution should be exercised in its use. It calls potassium into the blood stream and builds up the circulating blood volume by withdrawing the intracellular fluids. There is also apt to result an elevation of pulse pressure without a true rise of blood pressure. There is still no complete substitute for blood and sodium chloride in adequate amounts and appropriate proportions. In shock from hemorrhage, physiologic saline solution and adrenocortical extract should be administered first. Then, albumin or blood should be given. If blood banks are to be used, the depots must be very large, as evidenced by the giving of 14 liters of blood in thirty days to a patient with burns.

The discussion was opened by Dr. Walter B. Cannon, who compared some of the simpler early concepts of the mechanism of shock with those of the more recent observers. He asked whether isotonic albumin should be used rather than hypertonic, and also whether the potassium freed during the early stages of shock was enough to cause a fall of blood pressure. It was stated that some observers have not had good results with adrenocortical extract, whereas Katz, in Chicago, believes that desoxycorticosterone acetate may be helpful if given prophylactically. The question was raised concerning the advisability of using plasma alone in burns.

The discussion was continued by Dr. Kenneth Coonse, who emphasized the value of the early diagnosis and proper treatment of shock and minimized the question of potassium ion as a cause or effect of the phenomenon. It was pointed out that the histologic changes observed in the adrenal glands are also demonstrable in other organs and probably are not specific. Other organic extracts might therefore help at the appropriate time, but nothing will be of avail beyond a certain point.

Dr. J. E. Dunphy stressed the need for controlled fluid therapy rather than mere fluids. Potassium is probably not all important or even of primary advantage. Capillary permeability may be caused by the absorption of toxins from sepsis. The prime factor apparently is a discrepancy between the existing vascular bed and the circulating blood volume, and this may be brought about by a number of causes. An increase of the vascular bed may result from nervous impulses such as those following a high spinal anesthesia. Toxins may cause direct injury to the vascular system, and this seems to cause changes in the specific gravity of the blood and plasma protein secondary to the fall of blood pressure. Hematogenic shock, as seen in blood loss, does have initial changes similar to those described by Dr. Scudder. Adrenocortical extract has a rational basis and deserves a place in shock treatment, but should not be accepted as a cure-all.

In conclusion, Dr. Scudder emphasized the facts that adrenocortical extract was only one phase of the subject and that its use is absolutely contraindicated in shock from sepsis. One practical observation is that a continued increase of hemoconcentration in the presence of saline infusions indicates the approach of irreversible shock.

BOOK REVIEWS

The Autonomic Nervous System: Anatomy, physiology and surgical application. By James C. White, M.D., and Reginald H. Smithwick, M.D. Second edition. 8°, cloth, 469 pp., with 92 illustrations and 19 tables. New York: The Macmillan Company, 1941. $6.75.

The first edition of this book, written in 1935 by Dr. White alone, was well received and proved to be a valuable contribution to current medical literature. In six years, much has been added to knowledge of the autonomic nervous system by anatomists, particularly Ranson and Clark, by physiologists, such as Cannon and Fulton, and by surgeons, the two authors of this new edition being important contributors themselves. The book, nearly completely rewritten and vastly improved in its new form, is a fundamental text, invaluable to surgeon, neurologist, cardiologist and many others. The period between editions has given the authors time to revise the old and add the new; the publishers have fully co-operated, and physicians are presented with a complete, up-to-date treatise. The volume, like the first edition, is highly recommended.

Society and Medical Progress. By Bernhard J. Stern. 8°, cloth, 264 pp. Princeton, N. J.: Princeton University Press, 1941. $3.00.

This book was long overdue, and now that it has arrived, students of medical history and sociology will find it a valuable tool in the consideration of problems that directly concern medicine and society. The author, a social scientist of note, brings to the presentation of his material a broad background of intellectual knowledge, a keen understanding of medical problems and a penetrating analysis of the social factors that mold, and in turn are molded by, the advance of medicine. The reader is offered a stimulating review of the steps taken by medicine from its infancy to its present status. The tone of the narrative is heightened by a good account of the role of the medical schools and the development of the modern hospital. The subsequent chapters on urbanization, income and health, conquest of famine, medical advances and social progress and resistances to medical changes give a most graphic picture of the inevitably close relation that now exists between medicine and society.

One is a little disappointed at not finding reference to Zabdiel Boylston or W. T. G. Morton. Furthermore, to find on page 182 that the Warburton anatomical act of 1832 is referred to as the first of a series of laws in this connection is to overlook the fact that Massachusetts passed the first anatomical act in 1831. These points, however, are indeed minor.

A feature worthy of special note is the excellent bibliography for each chapter that is found at the end of the book. The reviewer is convinced that a book such as this one should be placed in the hands of all readers.